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PROGRESSIVE SCLERODERMA OF THE SKIN WITH CYSTIC SCLERODERMAL CHANGES OF THE LUNGS

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PROGRESSIVE scleroderma has long been recognized as a disorder of a general character. Apart from the skin and its appendages, the underlying musculature, the fascia, the tendons, the mucous membrane of the mouth and the bones and joints are also characteristically involved. The sclerotic changes are not restricted only to organs bordering on the skin, but, as evidenced by the autopsy records so far published, may be encountered in internal organs too. Thus Ehrmann [1] gave an enumeration of the internal organs concerned (esophagus, lungs, heart, kidneys, liver and incretory glands) and described their involvement in a way that leaves no doubt as to the specifically sclerodermal nature of the symptoms. Since that time, important evidence concerning the subject has been contributed by others too. Thus Podkaminskiy [2] described peculiar changes in bone and Weissenbach [3] functional disturbances of the esophagus associated with progressive scleroderma.

Characteristic pulmonary changes had already been referred to by Finlay,[4] who drew attention to the relationship existing between bronchitis and solidification of the pulmonary tissue, on the one hand, and sclerodermal disturbances of respiration, on the other. Von Notthafft [5] described an increase in the amount of interalveolar connective tissue as well as extensive changes of the blood vessels.

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1. Ehrmann, S.: Sclerodermie, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, pp. 804-819.

2. Podkaminskiy, N. A.: Acrosclerosis Hyperplastica Intraossea, Am. J. Roentgenol. **38**:889-892 (Dec.) 1937.

3. Weissenbach, R. J., and others: Sclérodermie progressive: Syndrome de Thibierge-Weissenbach; ulcère de jambe et calcification en molletières; troubles oesphagiens, Bull. Soc. franç. de dermat. et syph. **44**:2018-2024 (Dec.) 1937.

4. Finlay: Scleroderma, Middlesex Hosp. Rep. (1889), 1891, p. 29; cited by Luithlen, F., in Mraček, F.: Handbuch der Hautkrankeiten, Vienna, A. Hölder, 1904, vol. 3, p. 152.

5. von Notthafft, A.: Neuere Arbeiten und Ansichten über Sclerodermie, Centralbl. f. allg. Path. u. path. Anat. **9**:870-960, 1898.

Matsui [6] found, at 6 autopsies, sclerodermal changes of the lungs and Kraus,[7] in 1 case, chronic interstitial pneumonia, with new formation of connective tissue and blood vessels, round cell infiltration and alveolar proliferation in gland fashion. In some of the patches the blood vessels showed pronounced thickening of the intima. Since that time, various publications have appeared dealing with the problem of a possible combination of tuberculosis and progressive scleroderma. In 1941 Murphy [8] reported peculiar roentgenologic changes of the lungs which he considered sclerodermal in nature. Weiss, Stead, Warren and Bailey [9] gave an account of sclerodermal changes of the lungs, evidenced by roentgen rays and autopsy.

In the following reports are described peculiar changes of the pulmonary tissue which were encountered in 3 cases of progressive scleroderma, reference to which has so far been made nowhere else in the literature.

REPORT OF CASES

CASE 1.—M. P. was a boy of 14, whom I saw for the first time on July 18, 1923, complaining of general weakness and uncontrollable cough and presenting painful ulcers over both lateral malleoli. Apart from measles, he reported nothing extraordinary in his history. A family history was not obtainable, since his parents had died early.

State on Admission.—The boy's face was rather stiff, the lips were thin, the mouth could not be completely opened, the nose was pale and pinched and the chin was strikingly small. The skin of the forehead was thin and shining and could be wrinkled only with difficulty. Whistling or laughing was impossible. His speech was blurred and of a nasal character. The tongue was atrophic, and there was occasional dysphagia.

Upper Extremities.—The hands were cyanotic, the skin of the fingers was indurated and sclerosed and flexing was difficult, the fingers were pointed and the nails were claw shaped. On the finger tips and the dorsal sides of the finger joints small ulcerations were noted. The skin of the forearms and the lower third of the upper part of the arms was leathery, thickened and smooth, could not be lifted and was tautly stretched over the osseous protrusions.

Lower Extremities.—The feet were cyanotic, and the skin of the legs was thickened, particularly in the region of the knee joint, on both sides, the mobility of the joints being restricted. On both lateral malleoli, there were circular ulcerations about 1.5 cm. in diameter, which were extremely painful, covered with a

6. Matsui, S.: Ueber die Pathologie und Pathogenese von Sclerodermia universalis, Mitt. a. d. med. Fak. d. k. Univ. zu Tokyo **31**:55-116, 1924; cited, Presse méd. **2**:142, 1924.

7. Kraus, E. J.: Zur Pathogenese der diffusen Sklerodermie, Virchows Arch. f. path. Anat. **253**:710-734, 1924.

8. Murphy, J. R.; Krainin, P., and Gerson, M. J.: Scleroderma with Pulmonary Fibrosis, J. A. M. A. **116**:499-501 (Feb. 8) 1941.

9. Weiss, S.; Stead, E. A., Jr.; Warren, J. V., and Bailey, O. T.: Scleroderma Heart Disease, with Consideration of Certain Other Visceral Manifestations of Scleroderma, Arch. Int. Med. **71**:749-776 (June) 1943.

smeary discharge, with thin cyanotic edges, and surrounded by an inflammatory halo.

Trunk.—The skin of the chest had a sallow, yellowish tinge, the musculature of the thorax was atrophic and only with greatest difficulty was the patient able to lift his arms. The skin was tightly stretched over the bones but could be creased. No sclerotic changes could be palpated here. Both testicles were small, like those of a 5 to 7 year old boy. There were no hairs in the pubic and axillary regions. The patient complained of constantly feeling cold and, further, of general weakness, and he was troubled by a sort of dry, irritating cough. Blood counts were normal, the urine was also normal and the Wassermann reaction was definitely positive, but there was no indication that the patient had ever had syphilis. With reference to the pulmonary symptoms, medical and roentgenologic opinions were in agreement as to their being of a tuberculous nature, although there were no bacillary findings.

Specific antisyphilitic treatment, which was started in 1926 and 1927, effected no improvement of the sclerodermal symptoms.

Histology of the Skin.—Hand: The epidermis was slightly atrophic and the fibrils of connective tissue in the papillary and adjacent layers of the corium slightly thickened. In the rest of the corium, one could see thick, hyaline connective fibrils containing a fairly great number of cells. In the subcutis, in the midst of the panniculus, there were large hyaline fibrous islets. The vicinity of the sebaceous glands and hair follicles was free from sclerosis. The bands in which the blood vessels were embedded contained a fair amount of cells. The endothelial cells of the blood vessels were increased in number, in some places distinctly bulging toward the lumen. A few lymphocytes and leukocytes were seen in the perivascular tissue. Between the hyaline bands, there were fairly abundant, wavy, elastic fibrils stretching across all the layers of the corium.

Second Admission.—When, in May 1930, the patient reported again, he was even worse with reference to his general condition as well as to the cutaneous symptoms. The sclerosed skin was firmly attached to the underlying tissue, and it was dry and parchment-like, surrounding the body like a cuirass. The mouth could be opened only with difficulty, and there was uncontrollable cough. The patient, who was now 21 years old, made a eunuchoid impression (no hair, atrophic testis and penis and falsetto voice). In May 1932 he was admitted to the hospital, as he was then suffering from dyspnea and weakness, where he died after six days of anuria and dyspnea.

Postmortem Examination.—Autopsy revealed cystic lungs, scleroderma of the skin, chronic enlargement of the spleen, coalescent patches of fatty infiltration of the liver, atrophy of the adrenals, fatty infiltration of the kidneys and cerebral anemia. The extraordinary findings of the lungs were the subject of special investigations by Getzowa [10] and are only briefly outlined.

The lungs, which had been preserved in toto in solution of formaldehyde, presented the following status (Getzowa): The volume of both lungs was reduced and the pleura thickened, showing the remnants of fibrous adhesions, except for the apexes and the hilar regions. On both sides, the individual lobes had grown together and were also attached to the diaphragm. The adhesions between the individual lobes occupied areas of up to 2 cm. in diameter and were apparently of an earlier date. There were cysts of about pea size, close together and shining through the thickened pleura.

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10. Getzowa, S.: Pulmosclerosis Cystica and Pulmosclerosis Compacta in Scleroderma Progressiva, Arch. Path. **40**:99-106 (Aug.) 1945.

Cut Surfaces: Paravertebral section through the left lung, running through the upper and lower lobes. In the lower lobe there was a peripheral cystic layer bordering on the pleura, of 2.5 to 3.5 cm. in width; in the neighborhood of the diaphragmatic part of the pleura it was narrower (1 to 2 cm.). The borderline between the cystic and noncystic parenchyma was sharp and jagged, small cystic areas protruding into the noncystic tissue. The central region, that is, the entire hilar region, contained no cysts. The majority of the cavities were about the size of a pinhead, intermingled with larger cysts, up to about 1.5 cm. in diameter. The

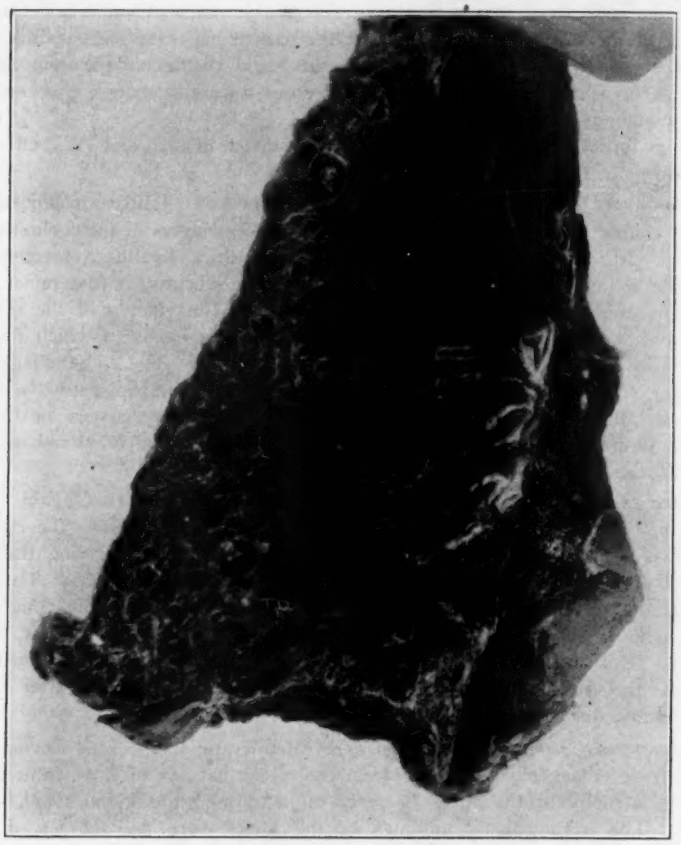

Fig. 1 (case 1).—Distribution of cysts, occupying the peripheral portions of the lower lobe of the lung, with omission of hilar region.

size of the cysts showed no dependency on localization, a few larger ones occurring near the center and others in the subpleural area. The cysts were close together, separated from each other by narrow septums. In the upper lobes, the apexes contained no cysts, while anteriorly there was in some places a narrow cystic layer (0.5 to 0.6 cm. wide). Higher up, the cystic areas were unevenly and discontinuously distributed as isolated islets.

Paravertebral section through the right lung: The lower lobe (fig. 1) presented the same picture as the left one, containing a peripheral cystic layer, occasionally

thicker than that on the left. Most of the cysts were pea sized, except for a few which had the size of a bean. The hilar region was free. The borderline here was also sharp. In the upper lobe the apex was also free from cystic changes; otherwise there was the same peripheral cystic layer as on the right, spreading to the central lobe too.

In view of the aforementioned pathologic changes, the roentgenograms could now be interpreted differently (Druckmann). Roentgenologically, there were numerous, in the majority small but also occasionally large, opacities of the pulmonary field. There was greatly reduced air content. Scattered all over both lungs, there were both small and large (up to over pea sized) circular light patches. There were homogenous shadows over both apexes.

Résumé.—The pulmonary tissue seemed to have been replaced by fibrous tissue containing numerous cavities. There were extensive adhesions, particularly in the upper portions. There was enlargement of the heart in all directions, with no special configuration.

Summary of Case History.—The patient, who had been under clinical observa- for about nine years, presented progressive scleroderma with acrosclerosis, dyspnea and cough, general weakness and eunuchoidism. Autopsy revealed extensive fibrosis of the lungs, with cyst formation and with omission of the apexes and central pulmonary portions. There were, moreover, extensive pleural adhesions, splenic enlargement, fatty degeneration of the liver and atrophy of the adrenals. The heart was found enlarged, but the cardiac findings can be considered to be the result of impaired pulmonary circulation owing to impairment of respiration by fibrosis of the lungs.

CASE 2.—The patient, P. S., was a woman of 34, who reported no earlier disease worth mentioning. Eleven years before she consulted us she had had a normal delivery, and two years before we saw her she had been treated with ovarian preparations for dysmenorrhea. She suffered from depression and was extremely emaciated (she had lost 25 Kg. during the past two years). In the summer of 1938 she had had pain of the joints, and in September 1938 cutaneous changes had started making their appearance, which rapidly became intensified and were accompanied with severe ankylotic changes of the joints. She was admitted to hospital in September 1939.

State on Admission.—The patient was extremely thin, her face was stiff and expressionless and the skin was tautly stretched over osseous protrusions. The nose was pinched, the chin was small, around the mouth there were radiating wrinkles, the lips were thin and the skin was pigmented. The auricles were so thin that one could see the cartilage shining through. Only with difficulty was she able to wrinkle her forehead, and she could not open her mouth completely. The tongue showed atrophy, with white atrophic bands also running down the hard and soft palates. The skin of the neck was pigmented and striped and had a senile appearance. On the trunk the skin was slightly thickened and included large pigmented areas. The pathologic changes were particularly pronounced on the extremities, especially on the arms. On the forearms and hands, the skin was firmly attached to the underlying tissue. The hands were small and the fingers claw shaped. The finger joints were practically immobile, and there were small ulcerations on the back of the joints. The nails were deformed and atrophic. The musculature of the upper extremities was also atrophied, and in all joints flexion was restricted. As to the lower extremities, the skin of the feet was cyanotic and showed hyperpigmentation. At the posterior, lower parts of the thighs, there were sclerosed patches in triangle shape, and in these areas the mobility of the joints

was also restricted. Roentgenograms of the bones showed atrophy, but otherwise they were normal. Results of urinary examination and of chemical analyses of the blood were normal. Blood counts showed erythrocytes 3,700,000, hemoglobin content 60 per cent and leukocytes 6,200 (polymorphocytes 84 per cent, lymphocytes 10 per cent, monocytes 5 per cent and Türck forms 1 per cent); there was anisocytosis; the basal metabolic rate was plus 7 per cent, and blood phosphorus was 2.7 mg. per hundred cubic centimeters. For calcium determinations the quantity of blood available was insufficient. Roentgenograms of the lungs (Druckmann) showed increased pulmonary markings on both sides.

The patient underwent parathyroidectomy and, later, sympathectomy (Prof. Mandl), which, to begin with, to some extent relieved the articular as well as the sclerodermal symptoms. Then the condition became stationary, to deteriorate later, with the advent of ulcerative stomatoglossitis and diarrhea, and the patient eventually succumbed to the disease.

Autopsy Record (Gelly, of the Pathological Institute, Head, Professor Franco).—1. There was scleroderma, and all joints of the hands and feet and knees and elbows were ankylosed. 2. In the lungs there was alveolar distention, occasionally assuming cystic dimensions in the cortical and subcortical layers of the upper and central lobes on the right and even more pronounced in the inferior lobes. There was atelectasis of the inferior lobes, slight hydrothorax on both sides and pulmonary edema. 3. There was nephrolithiasis on the right (gravel), with cloudy swelling of the kidneys. 4. Diffuse ulcerative colitis (amebic dysentery?) was present. 5. Small ovarian cysts were found.

In view of the peculiar nature of the pulmonary findings I am giving the full record of the respiratory organs. The gross appearance of the trachea and main bronchi was normal.

Left Lung: The left lung was globe shaped and heavy. The lateral surface showed a number of fine, tough films, by which the lung had originally been attached to the thoracic wall (adhesions). The cut surface of the upper lobe showed a uniformly rosy color. On the vertebral surface, there were two parallel bands of 1 to 2 cm. in width, recognizable through the pleura as consisting of big air bubbles. On the cut surface, one could see a broad, superficial band, of distinct alveolar enlargement, containing a few cysts too. The parenchyma showed normal air content, apart from the aforementioned portions, pieces of which sank in water.

In the inferior lobe, the cut surface was uniformly dark red and contained no air. In certain areas, 2 cm. beneath the pleura, the parenchyma was converted into one big mass of cystic cavities of varying size (from the size of a pinhead to that of a pea). The rest of the parenchyma had a fleshy appearance. Small pieces of the aforementioned areas and of the parenchyma, apart from that in the neighborhood of the cysts, sank in water.

Right Lung: The right lung was heavy and globe shaped. The superior and central lobes were elastic. On the lateral surface there were fine red films. The cut surface of the inferior lobe had a dark red appearance. In this area, too, and also in the cortical zone one could see numerous small cavities, similar to those found in the left lung. The rest of the parenchyma had a fleshy consistency and sank in water. The small intrapulmonary bronchi were normal to the naked eye.

Summary of Case.—In this case scleroderma had set in at the age of 34 and was accompanied with ovarian disturbances. The leading symptoms were diffuse scleroderma of the skin, with some additional circumscribed sclerodermal areas, acrosclerosis, polyarthritis and ankylosis of joints. On autopsy, the picture was similar to that presented by case 1, showing, although to a lesser degree, the same cystic sclerosis of the lungs, in this case too with omission of the apexes.

The peculiar pulmonary changes revealed by autopsy in the 2 aforementioned cases make it easier to give the correct interpretation to the clinical symptom presented by the third case.

CASE 3.—The patient, A. P., was a woman aged 21. She called on the outpatient department in 1925, presenting symptoms of scleroderma on various parts of her body, which she reported to have had since her seventeenth year. She had, since that time, been under constant medical supervision. As it was assumed that she was suffering from pulmonary tuberculosis, she was at the same time treated at the medical department. In her history, there was nothing extraordinary. The menses were irregular.

State on Admission (May 12, 1939).—The patient was a slenderly built girl, weighing 40 Kg. The skin of her face showed diffuse pigmentation and was thin and tautly stretched over osseous protrusions. The nose was pinched and the forehead smooth, wrinkling only with difficulty. Whistling was also difficult. Around her mouth there were small radiating wrinkles of the skin, which lent her face a senile appearance, extremely striking in such a young girl. The ears were small and the skin over them smooth, shining and taut and covered with milium-like efflorescences. The chin was small and made an atrophic impression. Numerous telangiectases were covering the skin of the neck, which was atrophic, including bands of depigmentation arranged in necklace fashion. On the nape of the neck, patches of atrophic skin with depigmentation could be seen. Numerous telangiectases were also present on the chest. The musculature of the shoulder regions was atrophied, and lifting as well as abduction of the arms was definitely restricted.

Upper Arms: There were numerous telangiectases, being so numerous and close together on the dorsal part that they created the impression of erythema. At the olecranon, there were depigmented plaques 2 cm. in diameter.

Forearms: The skin, which was firmly attached to the bones, showed a profusion of hyperpigmented and vitiligo-like patches.

Hands: The hands were small, and the skin was firmly attached to the underlying tissues, showing depigmented plaques with pigmented inclusions. The fingers were indurated and immobile, and the distal phalanges were atrophied. On the first and fourth fingers of the left hand, there was mutilation of the distal phalanges. The fingers were held in a slightly clawlike fashion.

Thighs: On the thighs the blood vessels were decidedly protruding, while the skin itself was soft and showed no atrophy. Over the knee joints, there was induration of the skin, with some scattered patches of depigmentation. On the legs the skin was thin and shining. There were depigmented scars on both malleoli, indicating the place where ulcers had been present, on account of which the patient had already spent some time at our department on an earlier occasion.

Feet: The feet were small and cyanotic, with phalangeal and plantar clavi.

Secondary Sex Organs: The sex organs were normal. The menses had stopped at the age of 30.

Histology of the Skin: The epidermis showed slight atrophy. The papillary layer and the underlying tissue consisted of loose-meshed connective tissue. The corium was extremely thickened. There were hyaline, fibrous bands containing few cells and showing basophilia. There were small perivascular infiltrations, consisting of neutrophilic cells, including a few lymphocytes. The musculature surrounding the hair follicles was hypertrophic. The blood vessels were dilated and contained numerous leukocytes. The elastic fibers were everywhere well preserved.

Apart from the suffering caused her by the sclerodermal lesions of the skin (pain due to ulceration and inability to walk owing to the presence of clavi), for five years the patient had had difficulty in swallowing dry bits, which felt as though they were retained on the level of the incisura jugularis. At the time that she was examined by us, her chief complaints were her troublesome cough and general weakness.

In the sputum, no tubercle bacilli were found during the entire time. Reactions to tuberculin tests were likewise negative. The Wassermann reaction was negative. The creatinine level was 0.1 per cent and the creatine level 0.22 per cent. The

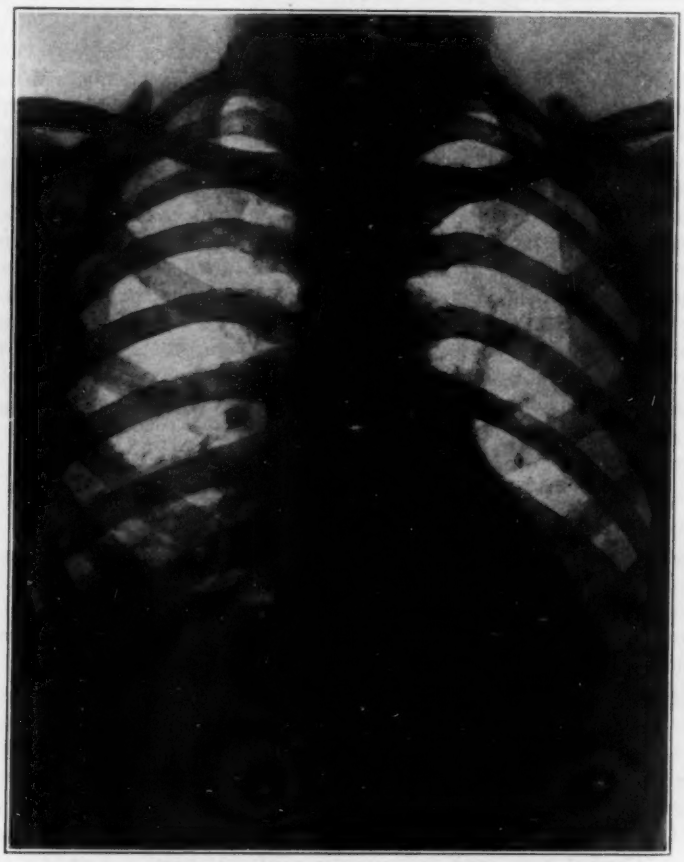

Fig. 2 (case 3).—Roentgenogram of the lungs taken in 1938. There is a suggestion of fibrosis and moderate bronchiectasis.

urine was otherwise normal. The roentgenograms of the lungs (Druckmann) showed, on Dec. 23, 1935, increased pulmonary markings and, on Sept. 9, 1938, opacities (fig. 2) surrounding the inferior hilar ramifications on both sides, intermingled with lighter patches (suggestive of cavities). The right side of the diaphragm was flattened, showing adhesions to the base of the lung. The roentgenologic findings as a whole were indicative of a moderate degree of bronchiectasis.

In November 1943, the patient was, on account of her pulmonary disease, examined by the physician of the Workers' Sick Fund (Steigbuegel), and, as there

was a suspicion of a specific disease, she was referred to a phthisiologist, who found extensive changes of the lungs. The following is his report (Huppert): In both upper lobes, especially on the left, there were band-shaped shadows of moderate intensity, partly interlaced, on both sides communicating with the hilus. In the left lower lobe, just above the diaphragm, there was an inhomogenous shadow with moderately sharp outlines (1.5 to 2 cm. in diameter). In the right apex, there was enlargement of the shadow accompanying the second rib. There was apical pleuritis, and there were lime depositions in both hili, particularly on the right. The apical regions showed no pathologic changes.

Summary: There were proliferative-fibrous changes of both upper lobes, with scattering to the left below. The findings are suggestive of remnants of a hematogenous tuberculous infection. There were no bacilli in the sputum (twice examined). Culture of the gastric juice likewise showed no organisms.

Roentgenograms taken on Jan. 18, 1944, yielded more or less the same picture.

Summary.—In a young woman, the development of progressive scleroderma could be followed up over sixteen years. The symptoms did not remain restricted to the skin but gradually spread to the mucous membrane of the mouth and esophagus (dysphagia). There were also pulmonary symptoms, manifesting themselves, particularly on hot, dry days, by a troublesome cough and creating the impression of tuberculosis, although bacillary findings were constantly negative. Roentgenologically, there was atrophy of the pulmonary parenchyma, appearing in the roentgenograms as opacities and bronchiectasis. In the phthisiologist's opinion, they were due to proliferative-fibrous changes, with dissemination as occurring in hematogenous tuberculosis.

COMMENT AND SUMMARY

The 3 cases outlined present the typical picture of progressive scleroderma, with acrosclerosis as the leading symptom. In all 3 there was, moreover, pronounced acromicria. As to hormonal disturbances, the patient in case 1 showed eunuchoid symptoms while patients in cases 2 and 3 were suffering from dysmenorrhea and amenorrhea. The sclerodermal symptoms appeared, apart from the skin, also on the mucous membranes of the mouth and esophagus (dysphagia). Pulmonary symptoms (cases 1 and 3) were the reason that the patients were treated for tuberculosis. The roentgenograms showed in all cases peculiar changes of varying intensity, the correct interpretation of which was only later possible on the basis of autopsy findings. In a personal communication by Getzowa, the pulmonary findings were summarized and the formation of sclerotic cysts in the lungs explained as follows: "Disappearance of alveoli in the parenchyma and replacement by bronchiolar proliferation have taken place, the latter becoming progressively subject to cystic distention. The disappearance of alveoli is caused by a fibrous process of the alveolar walls, with subsequent dissolution."

In addition to this picture, referred to by Getzowa as "pulmosclerosis cystica," there is still another type of pulmonary sclerosis, consisting in disappearance of alveolar parenchyma as the result of progressive interalveolar fibrosis without cyst formation—"pulmosclerosis compacta."

While our first case was characterized by cystic distention in the alveolar tissue, the second presented a combination of the two aforementioned types.

The histologic aspect, as it is described in Getzowa's paper,[10] makes it obvious that the primary changes must have taken place in the connective tissue, later involving the elastic system and only subsequent to this, secondarily—with advancing degeneration and disappearance of the connective tissue—the blood vessels. The lesions are similar to those occurring in the sclerosed skin. The aforementioned pathologic findings leave no doubt that in these patients the pulmonary process was of a sclerotic character. Pulmonary cyst formation and fibrosis are, therefore, evidently symptoms of the underlying disease.

The roentgenologic appearance as it presented itself in these cases as well as in those published in the literature is correctly interpreted in the light of the autopsy findings only if one realizes that the different roentgenograms reflect the various stages and phases of one and the same process. In case 1 roentgenograms for the initial stage of pulmonary involvement are not available. Clinically, the pulmonary symptoms, consisting in troublesome cough and chronic bronchitis, had been reported for nine years. A roentgenogram which gave an indication of the cystic lesions of the lungs was made four days before the patient died, so that in it autopsy findings coincided with those established on roentgenologic examination. A network of cavities seen in the roentgenogram reflects the cysts of the sclerosed lungs. In case 2 there were no clinical symptoms suggestive of pulmonary involvement, either subjectively or objectively. The roentgenograms showed increased pulmonary markings, i. e., only slight indications of fibrosis. Autopsy, which had in that case been performed three months after the roentgenograms were taken, already revealed fairly severe pulmonary changes, although not to the extent seen in case 1. There was cystic formation, on the one hand, and compact fibrosis, on the other.

In the patient in case 3, who is still alive, pulmonary symptoms are reported to have been present since 1928 and could be checked up roentgenologically. The picture which the lungs presented in 1935 showed lesions similar to those described by Murphy. The roentgenograms taken in 1938 already revealed extensive pulmonary involvement (fig. 2) and fibrosis in combination with bronchiectasis, thus making it understandable why this case (similarly to case 1) was mistaken for one of tuberculosis, although bacteriologic findings were constantly negative. The changes presenting themselves on roentgenologic examination in 1944 were of a more destructive nature. In this patient the correct interpretation of the findings was of greatest social-hygienic significance, as the patient was a kindergartner, and the question was raised whether one was allowed to let her continue working in this

capacity. But even the phthisiologist had to admit that in view of the pathologic-anatomic findings established in other cases, and, further, in view of the absence of parenchymal changes of the apexes and constantly negative bacillary findings, the patient had to be considered as free from tuberculosis.

The course as well as the intensity of the pulmonary disease was different in the 3 patients. In the same measure as the general sclerotic process is characterized by a progressive tendency, the sclerotic changes of the lungs are likewise of a progressive character, the time required for the development into the different stages varying as to the individual case. The initial pulmonary manifestations may be present for a long time, but it appears that their advance may sometimes be slow (as in case 3) and sometimes more rapid (as in case 2).

The pulmonary lesions outlined are, therefore, apparently the specific symptoms of the progressive sclerodermal syndrome, and if one may judge from the histories of the cases given in the foregoing paragraphs, cystic sclerosis and fibrous solidification, which were encountered in addition to cystic formation in the second case, are no rarity. These types probably represent the final stage of pulmonary sclerosis. The different pictures presenting themselves on autopsy or roentgenologically may, therefore, be representative of the different stages of development.

SUMMARY

1. Three cases of progressive scleroderma are reported on, all of them presenting acrosclerotic symptoms.

2. Varying degrees of roentgenologically identified lesions of the lungs of a sclerotic nature are described.

3. In 2 of the cases, fibrous and cystic changes of the lungs of a sclerodermal nature were found on autopsy.

Professor Getzowa (Pathological Institute) and Dr. Druckmann, head of the X-Ray Department of the Hadassah University Hospital, Jerusalem, Palestine, gave assistance and placed the photographs at my disposal for publication.

UNUSUAL DERMATOSIS SIMULATING LICHEN PLANUS AND LICHEN CORNEUS HYPERTROPHICUS

Report of Six Cases

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THE FOLLOWING cases of a dermatosis simulating lichen planus and lichen corneus hypertrophicus are reported because they appear to be unusual and because they are, as far as I know, the first to appear in the Mediterranean theater of war, among American troops. In none of these cases had the patients been in the Southwest Pacific theater.

REPORT OF CASES

CASE 1.—A 20 year old Mexican-American soldier was admitted to the Twenty-Sixth General Hospital on Oct. 12, 1944, at which time he stated that two weeks prior to admission his palms suddenly became hard, thickened and fissured. They became progressively worse for about one week. Since then, their condition had remained unchanged. About three days previous to admission, an eruption also appeared suddenly on the arms and legs, the dorsa of the hands, the trunk, the face and the ears. This eruption also remained unchanged after it first appeared. Only the legs itched. The patient did not know when he started to lose the nail of the middle finger of the right hand, and he was not aware of the scaling of his scalp until it was called to his attention on hospitalization. No vesicular eruption preceded any of the lesions present on admission. The patient had had the usual diseases of childhood. A wisdom tooth was removed in July, 1944. He took quinacrine hydrochloride (atabrine) during the 1944 malaria season until October 20. He was an armorer and seldom came in contact with grease. He had been in the Foggia-Bari area of Italy since February, 1944.

Physical examination at the time of admission showed a diffuse, poorly demarcated, violaceous thickening of the palms, extending onto the wrists and the sides of the hands and covered with a thin white scale. There were a few intervening areas of apparently normal skin. The flexor surfaces of the fingers were similarly involved but to a lesser extent. The soles appeared thickened but of normal color. There was some loss of luster of the finger nails, particularly at the proximal ends, and the nail of the middle finger of the right hand was practically detached from its bed. There were violaceous papules over the dorsa of the hands and plaques and papules over the wrists and forearms and to a lesser extent over the rest of the arms and over the trunk. Part of the lesions on the inner surfaces of the thighs and legs were hypertrophic, and there was fusion of papules and plaques to form extensive lesions. Excoriations were present on the legs. There were papules on the dorsa of the feet. The interdigital spaces were clear. On and behind the external ears there were violaceous plaques. Along the creases of the eyelids there were

poorly defined violaceous thickenings. On the upper and lower lids of the left eye there were poorly defined, scaling, erythematous plaques. Throughout the scalp, but accentuated over the vertex, asbestos-like scaling was seen. There was a streak of pavement-like white thickening on the left buccal mucous membrane. On the right side, near the commissure, there was a white circular area.

A piece of tissue from the forearm was removed for biopsy. Microscopic examination showed moderate hyperkeratosis and an irregular thickening of the granular layer. There was irregular acanthosis with some edema, particularly in the interpapillary pegs. The basal membrane was gone, and the lower border of the epidermis was frayed. In the papillae and upper part of the cutis was a sharply demarcated round cell infiltrate. There were some dilated blood vessels in the papillae, and a few round cells had migrated into the epidermis. In the deep portion of the cutis there was a perivascular and periglandular round cell infiltrate. A few pigment granules were present in the epidermis as well as in the dermis. Tissue removed from the scalp for biopsy on October 20 was normal except for a light perivascular and periglandular infiltrate.

CASE 2.—A 39 year old white soldier was admitted to the Twenty-Sixth General Hospital on Sept. 11, 1944. He stated that one month previous to admission he had noted dryness of the hands. The palms and the flexor surfaces of the fingers and the radial border of the palms had turned white. The onset occurred over a three to four day period. About three weeks previous to admission, he had noted painful fissures on the finger tips, on the flexor surfaces of the wrists and in the webs between the thumbs and index fingers. On the palms themselves fissures developed a few days later. Next, verrucous lesions developed on the palms. About a week previous to admission, the heels became thickened, and a dermatitis developed on the legs. At the same time, the patient noted a plaque which appeared suddenly on his chest and did not change thereafter. He had mild pruritus of the legs. Otherwise, the dermatitis had not been pruritic.

The past history was negative for cutaneous disease, except for a severe sunburn suffered ten years previously while the patient was deep sea fishing. Immediately thereafter, achromic macular plaques developed on the scrotum, penis and pubic areas, together with some patches of canities of the pubic area and scalp. He had had measles and mumps. He had suffered for years from hay fever, for which he used nose drops.

He landed in French North Africa May 10, 1943, where he served until he was transferred to Italy in May 1944; since then he had been stationed in the Foggia area. The patient was a typist and clerk, both in the army and in civil life. He had taken quinacrine hydrochloride regularly during the malaria seasons of 1943 and 1944.

Physical examination at the time of admission showed a mild scaling of the scalp. The skin of the scalp was pink, and there were areas of baldness on both temples. There were pink plaques on the nose. There was a retiform whitish discoloration of the left buccal mucosa and some whitish discoloration of the lips. On the chest there was an erythematous and scaling plaque about 8 cm. in diameter. Similar but smaller plaques were present on the chest, shoulders and back. Over the perineum, penis and scrotum were plaques of vitiligo, and there were patches of white hair on the pubic region and the scalp. There was a scaling erythema with nodular thickening and with some fissuring on the palms. The skin of the heels was thickened and fissured. The legs and

arms were covered with a patchy dark erythematous scaling dermatitis. The distal ends of the finger nails were thickened.

Treatment consisted of daily injections of extract of liver and weekly injections of bismuth subsalicylate in oil. On October 14, typical lichen planus papules were observed on the trunk. These papules soon involved the extremities. A few appeared on the face, eyelids and neck, and pruritus developed. During the last week of October 1944, the patient had an irregular temperature up to

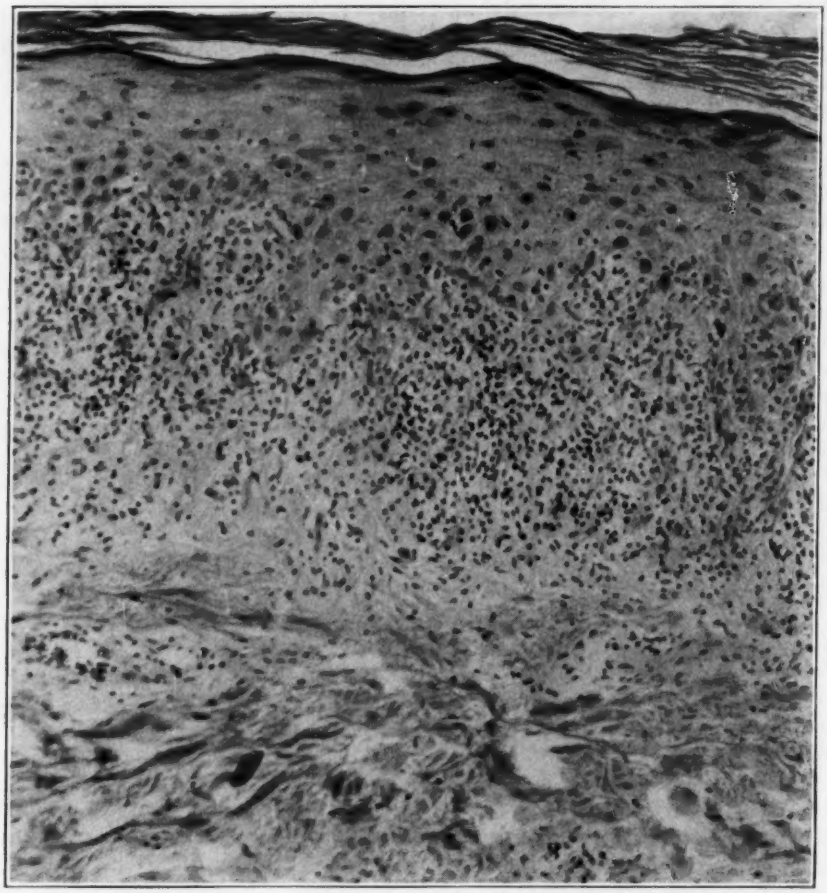

Fig. 1 (case 2).—Section from lesion on chest. It shows an irregular increase in the granular layer, leukocytes in the epidermis, indistinct basal layer, intercellular and intracellular edema. A well demarcated infiltrate of round cells is present high in the dermis and around the blood vessels and glands in the deeper layers. (Army Medical Museum negative 88859.)

103 F.; a general malaise developed, and the spleen became palpable and firm but not tender. In spite of the fact that three smears were negative for malaria organisms a diagnosis of malaria was made, and quinine therapy was instituted, with immediate cessation of symptoms. The eruption remained static after the generalized lichen-planus-like lesions appeared.

Physical examination when the patient was last seen, at the end of November 1944, showed essentially the same picture as on admission, except that lichen-planus-like papules had invaded the areas of discoloration of the chest, shoulders and back. There were typical lichen-planus-like papules on the trunk and extremities, and a few were present on the neck, face and eyelids. There was a partial separation of the nails at the distal border, and each nail had a depression one half to two thirds of the distance from the base. On some nails the plate was rough and uneven proximal to this line. Urinalysis gave normal results, and the Kahn reaction was negative. The sedimentation rate (Wintrobe) was 15 mm. in one hour. Roentgenologic examination of the chest showed no pathologic changes. The leukocyte count was 9,000 per cubic millimeter, with a differential count of 55 per cent neutrophils, 30 per cent lymphocytes and 15 per cent eosinophils.

Tissue removed for biopsy from the large lesion on the chest, September 13, showed hyperkeratosis and an irregular increase in the granular layer. There was irregular acanthosis, and leukocytes had migrated into the epidermis. The lower border of the epidermis was frayed, and there was some intercellular and intracellular edema. A round cell infiltrate was fairly well limited to the upper part of the dermis and the papillae but was present in a periglandular and perivascular distribution in the deeper parts of the cutis (fig. 1).

CASE 3.—A 37 year old white soldier first noted "little water blisters" on the dorsa of the forearms two months previous to admission to the hospital on Oct. 13, 1944. He was treated with calamine lotion by the unit surgeon, and the skin became dry. Little hard spots, about the size of the end of a lead pencil, appeared. These hard spots could be felt rather than seen and were the color of normal skin. The patient was given some ointment, which did not help. Three weeks after onset his hands, both dorsa and palms, became dry and cracked. There was no vesiculation previous to the eruption on the hands. He was admitted to one of the forward hospitals on Sept. 23, 1944, where his eruption was described as "erythematopapulosquamous, involving the hands, forearms and neck." He was given treatment, but the eruption continued to spread. The pruritus was not severe.

The patient gave no history of a similar eruption, and there was no family history of dermatitis. Koebner's phenomenon was not noted by the patient. He had come to Italy in April 1944 and had been taking quinacrine hydrochloride, 0.1 Gm. daily, all summer. He was an inspector of aircraft and did not come in contact with grease to any great extent. Before coming to Italy, he had spent twenty-seven months in the Aleutian Islands.

Physical examination at the time of admission showed that the palms were thickened, violaceous and scaly, with some fissuring. The skin of the dorsa of the hands and of the wrists was thickened, nodular and violaceous. The arms were similarly involved, with an accentuation of the eruption over the extensor surfaces of the elbows. There was some exudation on the radial surfaces of the forearm. The "V" of the neck was covered with an erythematous, scaling dermatitis, and there were plaques of a similar dermatitis on the trunk. The legs, thighs and buttocks were covered with an erythematous to violaceous scaling, nodular dermatitis, which became more pronounced toward the ankles. The soles showed some thickening but no distinctive color. There were poorly defined, erythematous, scaling plaques on the lower lids of both eyes. The scalp showed diffuse scaling. The mucous membrane of the mouth showed some leukoplakia-like changes, as did the lips. On the dorsum of the tongue were

several white circular lesions with absent or atrophic papillae. The glans penis showed no lesions. There was a mild separation of the distal ends of the finger nails.

During a month's hospitalization, the patient's cutaneous lesions did not show any decided change, although he took no quinacrine hydrochloride. The scale in the scalp became asbestos-like. A routine blood count was within normal limits (a differential count was not made), and the results of urinalysis were normal. The Kahn reaction of the blood was negative. The sedimentation rate (Wintrobe) was 7 mm. in one hour. Roentgenologic examination of the chest showed no glandular enlargement of the mediastinum. Tissue removed from the back for biopsy on October 14 showed hyperkeratosis with some plugging, thickening of the stratum granulosum and irregular acanthosis. There was washing out of the lower border of the epidermis and some infiltration of the epidermis with leukocytes. There was a fairly well demarcated infiltrate, predominantly of round cells, of the upper part of the dermis and of the papillae. There was also a light round cell infiltrate around some of the deeper blood vessels and glandular elements. The capillaries of the upper part of the cutis and papillae were dilated, and there was edema of this area. The prickle cell layer also showed some intercellular and intracellular edema.

CASE 4.—A 27 year old white soldier noted "warts" on the left ankle in 1934 after he had some sandburs in his shoe. The warts did not itch, and they had not changed since then. Early in August 1944 approximately 10 little lesions developed on his right arm. He described them as looking like bites. They did not itch and were never wet. In the middle of August 1944 he noted little blisters on the dorsa of the hands. A couple of days later his feet became involved, then his groin and buttocks and then his ears, and finally the eruption became generalized. He was treated at his squadron dispensary with soaks of potassium permanganate to the hands and feet and with ammoniated mercury ointment to his ears. He was admitted to a forward hospital Aug. 26, 1944, where he was treated with packs of solution of aluminum acetate locally and sulfadiazine by mouth for three days without improvement. He was transferred to the Twenty-Sixth General Hospital Sept. 1.

The patient was an aircraft mechanic. He landed at Oran, Algeria, in French North Africa, in February 1943 and went across North Africa to Bizerte, Tunisia, and on to Italy in December 1943. He took quinacrine hydrochloride during the summers of 1943 and 1944. He had the usual diseases of childhood, pneumonia in 1923 and an appendectomy in 1936.

Physical examination on admission showed an exudative dermatitis of the eyelids, ears, hands, buttocks, feet and legs. There was a vesicular follicular eruption of the trunk and an asbestos-like scale of the scalp. The tongue and buccal membrane, lips and anterior part of the hard palate were covered with a leukoplakia-like thickening.

The patient was given applications of a lotion of 5 per cent solution of coal tar N. F. to the body and alibour water (water containing zinc and copper sulfates) packs to the hands and feet, as well as a daily colloidal bath and injections of 2 cc. of concentrated extract of liver daily. The exudative dermatitis of the body cleared in about ten days. At that time there was noted the presence of generalized plaques, some of which were warty. Early in October violaceous polygonal papules were noted on the chest.

Physical examination at the height of the eruption showed the palms to be erythematous with a violaceous geographic area of thickening and hyperkeratosis.

The dorsa of the hands and the flexor surfaces of the wrists were violaceous and covered with elevated scaly plaques from a few millimeters to 1.5 cm. in diameter; these were more numerous on the flexor surfaces of the wrists, where they became confluent. Similar lesions were present on the extensor surfaces of the forearms and on the arms. On the chest were irregular, slightly elevated, dark erythematous plaques. A purplish postinflammatory blotchy pigmentation was present on the trunk. Elevated indurated scaly violaceous plaques and papules were scattered irregularly over the trunk. On the buttocks and in the intergluteal cleft were confluent verrucous scaling psoriasis-like plaques. The groin, penis and scrotum were similarly involved. The extensor surfaces of the knees were completely covered with confluent plaques like those on the buttocks (fig. 1). Similar plaques involved the dorsa and sides of the feet and ankles. The toe nails were normal, but the finger nails showed roughening of the nail plates, separation at the distal ends and deep depressions and opacities of the proximal ends. The mucous membrane still showed leukoplakia-like changes. The eyelids showed erythematous diffuse scaling. The scaling of the scalp was still present, and there was about a 50 per cent loss of hair. The ears were scaling.

Leukocyte and Differential Count on Examination of Blood of Patient Receiving Injections of Penicillin

Date	Hbg., Gm.	W.B.C.	Neutrophils, %	Lymphocytes, %	Eosinophils, %	Basophils, %
Nov. 10	15	20,000	54	14	32	..
Nov. 12	..	11,900	50	11	39	..
Nov. 14	..	14,000	38	16	45	1
Nov. 17	..	26,600	37	16	47	..
Nov. 20	..	22,000	24	16	60	..
Nov. 25	..	14,200	24	16	60	..
Nov. 28	14	11,400	18	19	63	..
Dec. 8	..	5,200	25	26	49	..
Dec. 12	..	.....	25	40	35	..

Treatment consisted of weekly injections of bismuth subsalicylate in oil. On October 28 gradually increasing doses of acetarsone were started. The lesions began to improve toward the end of October, probably spontaneously. On November 8, the patient became acutely ill with pain in the chest, cough, fever, expectoration and slight dyspnea. A diagnosis of pneumonia was made on November 9, and treatment with sulfadiazine was started. On November 10 there was no improvement, and injections of 25,000 units of penicillin every three hours was begun and continued until November 16, when the dose was cut to 15,000 units every three hours and finally the injection of penicillin was discontinued November 21. The penicillin was without dramatic effect either on the pneumonia or on the lesions. The leukocyte counts for this patient are presented in the table. When the patient was last seen, in the middle of December 1944, many of the verrucous lesions had undergone complete involution, leaving dark brown pigmented macular stains. All the lesions had undergone at least partial involution. The patient was given quinacrine hydrochloride, 0.1 Gm. daily, for the first two weeks in December without in any way influencing the dermatitis.

On admission, results of a routine urinalysis were normal. The leukocyte count was 6,750 (differential count was not made) per cubic millimeter. The hemoglobin content was 14.3 Gm. per hundred cubic centimeters of blood. The Kahn reaction was negative, and roentgenologic examination of the chest showed no evidence of mediastinal glandular involvement. The sedimentation rate (Wintrobe)

was 9 mm. in one hour. Tissue removed for biopsy from a lesion present on the ankle for ten years showed hyperkeratosis with parakeratosis. The stratum granulosum was absent. There was colossal acanthosis, some of the interpapillary pegs being slender, some clubbed and some bifurcate, so that the outline of the epidermis was very irregular. Leukocytes were present in the epidermis. The papillae were edematous, and dilated capillaries were present in the papillae and the upper part of the dermis. The infiltrate of plasma cells and round cells

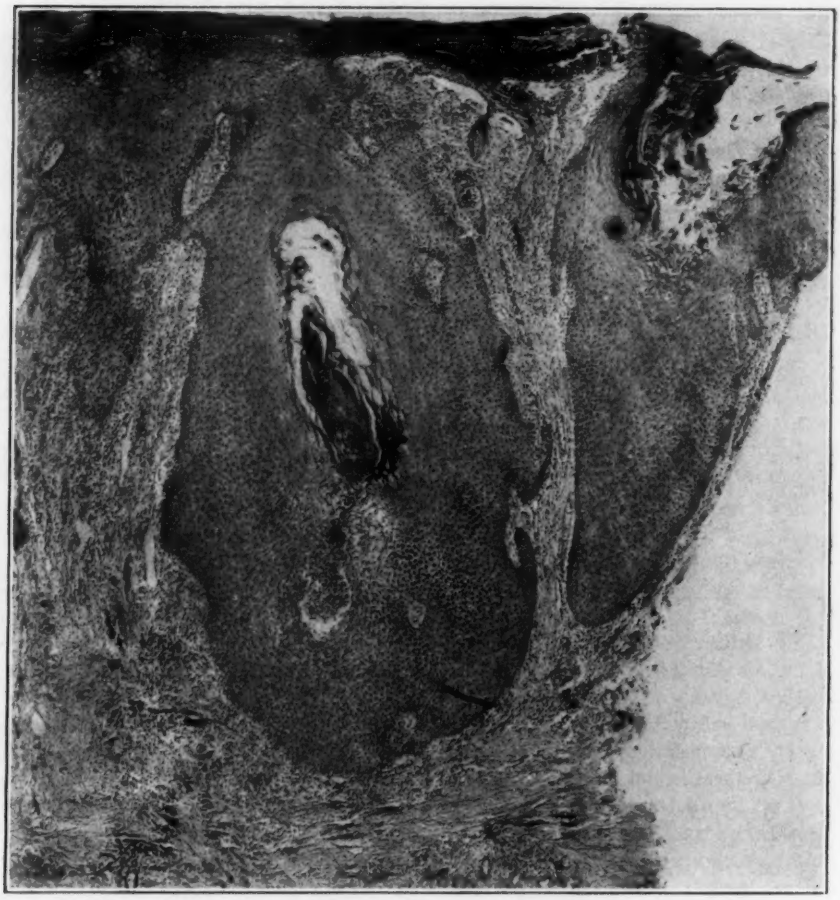

Fig. 2 (case 4).—Section from lesion on ankle. It shows hyperkeratosis, great acanthosis and irregular infiltrate in dermis. (Army Medical Museum negative 88864.)

was irregularly distributed in a perivascular and periglandular manner throughout the papillae and dermis and extended down into the fat of the hypodermis (fig. 2). A section removed from the thickened buccal mucosa on October 14 showed slight hyperkeratosis, an irregular thickening of the granular layer and irregular acanthosis, with migration of leukocytes into the epidermis and dilatation of the capillaries of the papillae and upper part of the dermis. The infiltrate was poorly demarcated. There was fraying of the lower border of the epidermis.

A lesion which was clinically a lichen planus papule was removed from the wall of the chest for biopsy on October 23. There were hyperkeratosis, irregular hypergranulosis and irregular acanthosis. There were a few migratory leukocytes in the epidermis, and the lower border of the epidermis was frayed. The blood vessels of the papillae were dilated, and there was a round cell infiltrate, rather

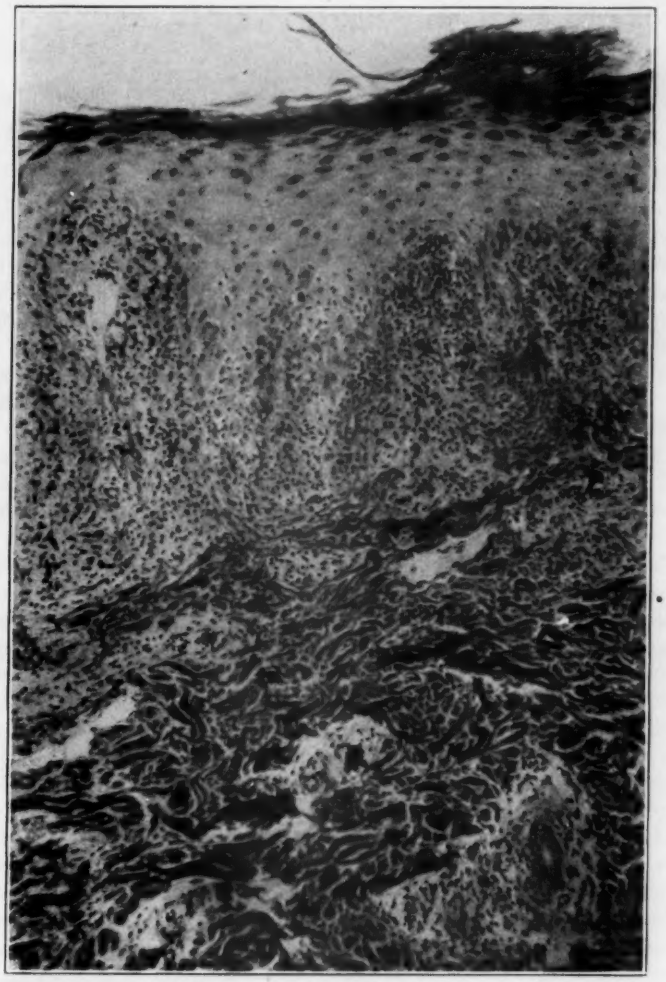

Fig. 3 (case 4).—Section from lesion on chest. It shows irregular increase in granular layer, basal layer indistinct and few leukocytes in the epidermis. A well demarcated infiltrate of round cells is present in the upper portion of the cutis, most pronounced around the blood vessels. (Army Medical Museum negative 89029.)

heavy, fairly well demarcated and accentuated perivascularly, in the papillae and upper part of the cutis. A slight perivascular and periglandular infiltrate was present in the lower portion of the cutis (fig. 3).

CASE 5.—A 32 year old white patient noted pruritus of the back of the hands in the middle of August 1944. The hands were not broken out at that

time. About two weeks after the pruritus began, the skin of the hands became thickened on both of the palms and the dorsa and fissures developed. The patient noted some swelling of the hands and arms, followed by the development of areas of dermatitis on the arms. At about the same time, he noted red spots on his chest and back. He also had an eruption about the nose, and his lips felt chapped. He was hospitalized in the forward area Sept. 28, 1944. While there, his thighs and legs became involved, some edema of the latter developing. He was transferred to the Twenty-Sixth General Hospital Oct. 16, 1944. The dermatitis was intermittently pruritic, increasingly so at night.

The patient was an aircraft mechanic. He had been stationed in the Bari-Foggia area of Italy since coming overseas. He gave no personal or family history of cutaneous diseases. He had taken quinacrine hydrochloride, 0.1 Gm. daily, during the summer of 1944.

Physical examination on admission showed a diffuse thickening and hyperkeratosis of the palms. The skin was diffusely scaling, red, dry and follicularly hyperkeratotic. The skin of the forearms and dorsa of the hands was thickened and scaling, and it had a violaceous erythema. The lateral surfaces of the arms were similarly involved. The skin of the chest anteriorly and of the front and sides of the neck was thickened, slightly scaling and erythematous. An asbestos-like scale was present in the scalp, thickest at the sides and thinning toward the vertex. The skin of the nose, of the adjacent areas of the cheeks and of the upper lip was thickened, scaling and erythematous and had a nutmeg-grater-like feel. There was slight erythematous scaling of the eyelids. On the trunk anteriorly as well as posteriorly were darkly erythematous scaling plaques, fairly well demarcated, 0.5 to 1.5 cm. in diameter; some were confluent. The thighs were diffusely erythematous and scaling, while their outer surfaces were covered with plaques like those on the trunk. The legs were scaling and erythematous, with poorly defined violaceous plaques 1 to 2 cm. in diameter. The soles were hyperkeratotic over the pressure points. There was slight interdigital maceration. The toe nails appeared normal. There were roughening and opacity of the proximal ends of the finger nails. The glans penis was clear. There were pavement-like white plaques on the buccal mucosa bilaterally and a diffuse white thickening of the anterior part of the hard palate.

The patient was given weekly injections of bismuth subsalicylate in oil. On November 7 gradually increasing doses of acetarsone were started. On November 10 he complained of soreness of the hard palate. Examination showed an eruption of sparse, small vesicles in the white thickened area of the hard palate, and there were two superficial ulcers on the palate adjacent to the molar teeth bilaterally. The administration of acetarsone was discontinued November 21.

When last seen, on Dec. 9, 1944, the dermatitis had taken on a brown color, particularly on the upper part of the thorax. The follicular hyperkeratosis in the areas of dermatitis was somewhat more pronounced, and the lesions on the back had developed a psoriasis-like scale which became powdery when scraped off and left no bleeding points. Deep rough depressions developed at the bases of all the nails except those on the fifth fingers bilaterally and on the first, second and third toes of the right foot. There were still a few areas of exudation on the right foot.

On admission, the result of a routine urinalysis was normal. The hemoglobin content was 12.8 Gm. per hundred cubic centimeters of blood, and the leukocyte count was 8,850 per cubic millimeter with 67 per cent neutrophils and 33 per cent lymphocytes. The sedimentation rate was 18 mm. in one hour (Wintrobe). Roentgenologic examination of the chest showed no mediastinal enlargement.

The Kahn reaction was negative. A patch test with quinacrine hydrochloride showed a doubtful reaction at forty-eight hours. Repeated scrapings and cultures of material from the interdigital spaces of the feet revealed no fungi. Tissue removed from a healing lesion on the trunk on December 5 showed two different types of reaction. Most of the section showed hyperkeratosis with one small area of parakeratosis. The granular layer was normal, as was the rete mucosa, except for some lengthening of the interpapillary pegs. The lower border of the epidermis was clearly demarcated. The infiltrate in the papillae and the dermis was for the most part perivascular, but in the deeper part of the cutis it was periglandular also. In one small part of the section there were hyperkeratosis, thickening of the granular layer, acanthosis, fraying of the lower portion of the epidermis, leukocytic infiltration of the epidermis and a well demarcated infiltrate of the upper part of the dermis. Throughout the section, there were pigment granules in the papillae and the upper part of the dermis.

CASE 6.—A 24 year old white patient noted the development of a few small vesicles on the inner aspects of the thighs in May or June 1943. These lesions were pruritic; he scratched them, and they oozed. He was given a lotion, which he used, with resultant disappearance of the lesions. A month later there was a recurrence of the dermatitis at the same location, this time in the form of grouped pustules. He again treated the eruption with a lotion, and there was almost complete involution in two months. In December 1943 the same type of lesions as he had on admission developed on the sites of the previous dermatitis and had not changed since except to increase slowly in size. Early in September 1944, lesions developed first on the right foot and then on the left foot. The hands broke out three weeks previous to admission; then there occurred eruptions on the neck, ears and penis. The attention of the patient was first called to the scaling of the scalp after his hospitalization. He was admitted to a forward hospital on Sept. 18, 1944, at which time his eruption was described as "papulo-squamous lesions on the thighs, hands and feet." He was treated with soaks of solution of boric acid, vitamins, colloidal baths and penicillin locally and systemically (300,000 units), with spread of the eruptions as previously noted.

The patient landed at Oran, Algeria, on Jan. 23, 1943 and crossed North Africa with his unit, leaving Bizerte, Tunisia, and landing at Naples, Italy, on Dec. 24, 1943. He was in the neighborhood of Constantine, Algeria, when the eruption broke out. He was a radio control operator. He took quinacrine hydrochloride regularly during the malaria season until he was hospitalized. The patient gave no history of a previous similar eruption affecting himself or his family. He had not had jaundice. Except for three attacks of pneumonia, his history was noncontributory.

Physical examination at the time of admission showed verrucous, violaceous, slightly indurated plaques on the medial surface of the left thigh. The plaques were covered with an imbricated, adherent scale which left no bleeding points on removal. There were several satellite plaques. There were an erythematous dermatitis of the dorsa of the hands and some nodules and areas of slight exudation. There was a similar erythema with nodules of the flexor surfaces of the wrist. The dermatitis stopped just above the wrists. There were a slight violaceous thickening of the palms and an erythematous dermatitis of the "V" and sides of the neck. An exudative erythematous scaling dermatitis was present on and behind the ears. The external auditory canals were free. The scalp showed an asbestos-like scale, most evident on the vertex. The soles showed an erythematous and scaling, sometimes verrucous, violaceous dermatitis in plaques,

worse on the heels and not related to pressure points. Areas of exudative dermatitis were present on the dorsa of the feet. On the penis there were lesions which looked like crusted ulcers. There was erythematous dermatitis of the back, with a tendency to follicular accentuation. The upper eyelids showed a slight violaceous thickening. The mucous membranes, including that of the

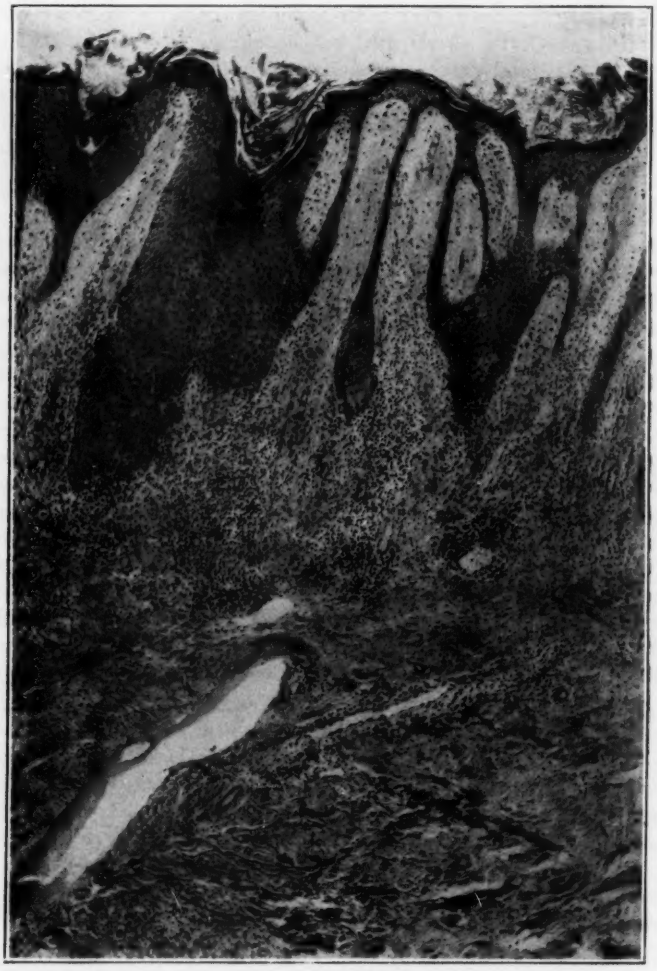

Fig. 4 (case 6).—Section from lesion on leg. It shows keratotic plugging and indistinct basal layer in areas. A round cell and plasma cell infiltrate is present in the upper portion of the cutis and around the blood vessels and glands in the deeper portions. (Army Medical Museum negative 89030.)

glans penis, were clear. The skin had a generalized yellow discoloration due to quinacrine hydrochloride.

The administration of quinacrine hydrochloride was discontinued as soon as the patient was admitted to the Twenty-Sixth General Hospital. He was given injections of bismuth subsalicylate in oil each week for nine weeks. During the

second week of treatment with bismuth, he was given gradually increasing doses of acetarsone. No therapy seemed to affect the dermatitis appreciably. Some areas of exudation developed at intervals, the area on the feet at times resembling a fungous infection. Early in November 1944 a patchy, scaly erythema appeared on the arms. In the involved areas the hair could be easily and painlessly removed. The eruption disappeared from the areas in four to six weeks, leaving them slightly depigmented. During the first two weeks of December 1944, the patient received quinacrine hydrochloride, 0.1 Gm. daily, with no exacerbation of the dermatitis.

On admission to the hospital the Kahn reaction of the blood was negative. Roentgenologic examination of the chest showed no pathologic changes. The sedimentation rate (Wintrobe) was 19 mm. in one hour. The hemoglobin content was 15 Gm., and the leukocyte count was 4,800. The results of urinalysis were normal. Repeated potassium hydroxide preparations of scrapings from the exudative lesions of the feet and from the patchy, scaly, erythematous areas of the arms disclosed no myceliums. A section from a piece of tissue, removed for biopsy from the leg on October 19, showed hyperkeratosis with a few areas of parakeratosis and some plugging. The stratum granulosum was irregularly present. Acanthosis was irregular. The interpapillary pegs were greatly elongated, some being slender, some clubbed and some bifurcate. There was a leukocyte infiltration into the epidermis. The lower border of the epidermis was well demarcated, except over the ends of some of the interpapillary pegs, where there was a suggestion of fraying. The blood vessels of the papillae and upper part of the dermis were dilated, and the papillae were edematous. The round cell and plasma cell infiltrate was heaviest in the upper part of the cutis but was present in the papillae and in the perivascular and periglandular areas throughout the dermis and extending into the subjacent fat (fig. 4).

COMMENT

The ages of the patients ranged from 20 to 39 years, which fairly well covers the age group of the enlisted men in the army. All these patients were nonflying enlisted men, although they were all air corps personnel. When first seen by me, they were all stationed in the Bari-Foggia area of eastern Italy. The primary lesions developed in 2 patients previous to their coming to this area (cases 4 and 6). None of the men had served in the Southwest Pacific, although 1 (case 3) had been in the Aleutian Islands for twenty-seven months before coming to Italy. In 4 of the 6 patients, the lesions were exudative at some time during the course of the disease. Itching varied from moderately severe to absent. In no case was it the primary cause of admission to the hospital.

No area of the skin was immune to attack. The palms, soles, scalp, hands, arms, legs and eyelids were involved in every case. The mucous membrane of the mouth, the skin of the trunk and the nails were involved in 5 patients (all except case 6). Other areas of the body were less often involved.

The sedimentation rate was normal in 3 patients and elevated (18, 18 and 15 mm.) in 3. A differential white blood cell count was made for only 3 patients, and for 1 of these 3 only after he had

contracted pneumonia. The blood of 1 patient showed no eosinophils (case 5), while that of 2 patients (cases 2 and 4) showed an appreciable increase in the eosinophils.

There were other cases of the same disease seen in the Italian theater among troops of the British Empire.[1] Those of us who saw the 6 patients whose cases are reported herein were at a loss as to how to classify their disease. Certainly some of the patients presented clinical lichen planus (cases 1 and 2). Others (cases 4 and 5) had what appeared to be a combination of lichen planus and great lichenification, and yet another (case 6) had great lichenification with nothing (except the lesions of the eyelids) in any way resembling lichen planus. Pautrier [2] stated that he had seen 15 cases of *lichenification verruquese (lichen corné hypertrophique)*, in 7 of which the patients had indisputable lichen planus in addition. He described the lesions of lichen corneus hypertrophicus as verrucous elevations which were located on the lower limbs, most particularly on the anterior surfaces, but which might also be observed on the thighs, buttocks, lumbar regions and, exceptionally, on the arms. The color was pinkish, reddish or brownish. The lesions were almost always covered with a dry and adherent scale, or with a corneous mass, grayish or brownish in color. The pruritis which accompanied the lesions was severe. The lesions illustrated in the article resemble lesions seen in my patients.

Microscopically, Pautrier found the picture to be that of lichen planus and/or lichen corneus hypertrophicus. In the latter he found enormous acanthosis with greatly enlarged interpapillary pegs. There was considerable, sometimes colossal, hyperkeratosis. The granular layer was thick but regular. The infiltrate was that of chronic inflammation and did not hug the epidermis. It was distributed irregularly in the skin. There were many greatly dilated blood vessels in the upper part of the dermis and the papillae; there was much edema of the papillae.

Darier [3] stated that he had repeatedly demonstrated the coincidence of lichen corneus hypertrophicus with typical lichen planus and with buccal lichen planus. He stated that the itching was variable. He had seen lichen corneus hypertrophicus develop on oozing or crusted eczematous foci, as did some of the lesions in 4 of the patients described herein.

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1. (*a*) Peterkin, G. A. G., and Hair, C.: Personal communication to the author. (*b*) Haswell, R. E., and Wilkinson, J. F.: Personal communication to the author. (*c*) Loewenthal, L. J. A.: Personal communication to the author.

2. Pautrier, L. M.: Les lichénifications anormales, Acta dermat.-venereol. **8**:313 (Jan.) 1928.

3. Darier, J.: A Textbook of Dermatology, translated by S. Pollitzer, Philadelphia, Lea & Febiger, 1920, p. 140.

Two of the patients presented (cases 1 and 2) would have been accepted as suffering from slightly precocious lichen planus had they not been admitted to the hospital at the same time as the other patients. Clinically, these patients had lichen planus, but in both cases the lesions developed much more rapidly and became much more verrucous than does typical lichen planus. In case 3 a lichen planus-like dermatitis developed following an exudative dermatitis of the forearms, and, although the clinical picture at the time he came under my observation was that of a severe lichen planus, there was some exudation of the forearms. Microscopically, the picture in the first 3 patients resembled that of lichen planus except for the invasion of the epidermis by leukocytes and a round cell periglandular and perivascular infiltrate in the deep part of the cutis. In case 4 the initial lesions apparently developed after trauma in 1934. New lesions developed following a generalized nonspecific exudative dermatitis of undetermined cause in 1944. The lesions were verrucous and violaceous and were covered with a thick scale; microscopically they showed hyperkeratosis, slight parakeratosis, acanthosis with elongation and clubbing of some of the papillary pegs, dilatation of the blood vessels of the papillae and edema of the papillae. There was a round cell infiltrate of the cutis, more pronounced in the upper layer and present in the papillae. The granular layer was inconstantly present. It was only after the eruption had been present for some weeks that papules clinically resembling lichen planus appeared on the chest. Microscopically, these papules showed the same picture as did the lesions from the first 3 cases. In case 5 the patient presented a generalized dermatitis with localized violaceous nodules and plaques and with follicular hyperkeratosis, the latter becoming more evident as the dermatitis subsided. There was also pavement-like thickening of the buccal mucosa and diffuse thickening of the mucous membrane of the anterior portion of the palate. The microscopic picture of the skin taken from a healing area on the trunk showed an area not essentially different from that of the lichen-planus-like papules removed from the first 4 patients. Adjacent to this area were areas that looked as though they could be regressing giant lichen. The patient in case 6 had no lesions of the mucous membrane and no lesions resembling lichen planus, other than slightly violaceous plaques of the eyelids. His lesions were primarily exudative and remained so, to a greater or lesser degree, while he was under my observation. The microscopic picture was that of giant lichenification, the same as the verrucous lesions of the patient in case 4. While the clinical and microscopic pictures of these patients differ somewhat from those of lichen corneus hypertrophicus as described by Pautrier,[2] the dermatosis in cases 4 and 6 would seem to fall in this category. While the other 4 cases are not instances of classic lichen planus, they more

closely resemble this dermatosis than any other with which I am acquainted. In case 4, also, there was clinical and microscopic evidence of this disease.

The cause of the eruption was not determined. Quinacrine hydrochloride was suspected but the suspicion could not be proved. Five patients had been taking quinacrine hydrochloride when the dermatitis broke out, and the sixth (case 4) was taking the drug when the dermatitis became generalized. The patient in case 6 was not taking quinacrine hydrochloride in December 1943 when the verrucous dermatitis developed, but he had been taking it at the time that the preceding exudative dermatitis developed and he was taking it when new lesions appeared in September 1944. Senear, Caro and Stubenrauch [4] presented before the Chicago Dermatological Society in February, 1944, 2 patients, a husband and wife, in whom there developed violaceous papules and nodules over the forearms, arms, legs, thighs, hips and buttocks shortly after they started to take quinacrine hydrochloride. The patients had been taking quinine for some time previously without any adverse effects. Some of the patients of Peterkin and Hair [1a] showed an exacerbation of the dermatitis while taking quinacrine hydrochloride. Haswell and Wilkinson [1b] were unable in 10 instances to reproduce the eruption with daily doses of up to 0.3 Gm. of the drug. I gave 2 patients quinacrine hydrochloride, 0.1 Gm. daily for two weeks, without in any way influencing the eruption. Patch tests with the drug elicited negative reactions in 5 of my 6 patients. In case 5 a slight erythema developed after forty-eight hours.

The hypothesis that the dermatitis develops on predisposed skin is attractive but valueless, since the cause of the predisposition, as well as the precipitating factor, is not known. The primary lesions in case 4 were apparently precipitated by the irritation of a sandbur in the shoe. The secondary lesions occurring while the patient was in the hospital, ten years after the primary lesions, may well have been precipitated by the exudative dermatitis which preceded them. The same may be said of the exudative dermatitis which preceded or occurred during the course of the dermatosis of 3 of the other patients, but it does not explain the generalized distribution of the lesions except in case 4, in which the exudative dermatitis was generalized; nor does it explain the occurrence of the dermatosis in the first 2 patients, who at no time had any dermatitis other than the lichen-planus-like lesions. Haswell and Wilkinson [1b] showed me a patient in whom the lesions developed in the site of a healed scabies, and Loewenthal [1c] showed me a patient in whom the lesions developed in exactly the

4. Senear, F. E.; Caro, M. R., and Stubenrauch, C. H.: Lichen Planus in Husband and Wife, Arch. Dermat. & Syph. **51**:353 (May) 1945.

locations of healed tinea. Myceliums had been demonstrated from the original lesions.

Quinacrine hydrochloride can cause a generalized exfoliative dermatitis,[5] and a fixed drug type of eruption [5b] with a violaceous color, both of which could be reproduced by the taking of the drug.[5b] The results of experimental readministration of the drug to patients suffering from the dermatosis under consideration are not uniform. Peterkin and Hair [1a] reproduced the eruption, while Haswell and Wilkinson [1b] and I were unable to do so. It is recognized that the inability to reproduce the eruption by readministration of the drug does not rule out the drug as the cause of the eruption. It is a well known fact that some people cease to be abnormally reactive to a drug after a time or during the actual administration of the drug. Perhaps such a circumstance occurred in these cases, but, if such a thing did occur, the high percentage of patients who became able to tolerate the drug is most unusual.

These patients were seen toward the end of the malaria season, after they had been taking quinacrine hydrochloride for some months, and a considerable amount of the drug should have been stored in the skin as well as in the other organs; however, the eruption progressed, even after the use of the drug was discontinued and the store of quinacrine hydrochloride should have been decreasing or should have entirely disappeared. It is possible that the mere presence of the drug had altered the capacity of the skin of the hypothetically predisposed patients to react, but this too would be difficult or impossible to prove.

SUMMARY AND CONCLUSIONS

Six cases of an unusual dermatosis are presented. The eruption may be primarily either exudative or dry and may resemble lichen planus, lupus erythematosus, psoriasis or a verrucous dermatitis. No area of the body surface is immune. Histologically, the lesions resemble either lichen planus or papillomatosis, with hyperkeratosis, acanthosis and a lymphocyte and plasma cell infiltrate in the papillae and dermis. One patient may present all, or any combination of, the clinical and histologic types. The cause of the disease has not been determined, but it is likely that quinacrine hydrochloride (atabrine) is in some way associated with the outbreak of the dermatitis. No satisfactory classification was found for the diease.

Present address: 1520 Chapala Street, Santa Barbara, Calif.

5. (*a*) Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1943, p. 141; (*b*) Nelson, L. M.: Dermatitis Due to Atabrine, to be published.

ICHTHYOSIFORM CHANGES OF THE SKIN ASSOCIATED WITH INTERNAL DISEASES

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MOST cases of ichthyosis are congenital in origin. A hereditary tendency has been noted repeatedly. Gray[1] postulates that the horny overgrowth is an attempt to compensate for the protection usually supplied by the oily secretions.

Acquired ichthyosis is rare but cases do undoubtedly occur. Such were described by Crocker,[2] who also mentioned the ichthyosis which is liable to afflict the Piper methysticum chewers of the Sandwich Islands. Little additional information is given by the Suttons,[3] who quote from Crocker.

Trophic changes, consisting of dryness of the skin, atrophy, hyperkeratosis and alopecia, are seen not infrequently in Hodgkin's disease. Ronchese[4] has described such a case. An ichthyosiform atrophy of the skin developed in a patient with lymphadenoma while he was in apparently good health, eleven months before his death. The changes took only six weeks to mature and were widespread. The cutaneous surface became rhomboidal scales with flaky edges, such as are seen in mild ichthyosis or in senile ichthyosis. Biopsy of the skin showed atrophy and hyperkeratosis, with no evidence of infiltration with Hodgkin tissue.

Identical changes were found in a patient reported by us.[5] The man, a fisherman with Hodgkin's disease, noticed night blindness before the

From the Department of Clinical Medicine, University of Edinburgh, and the Polish School of Medicine, Edinburgh.

1. Gray, A. M. H., in Price, F. W.: Textbook of the Practice of Medicine, ed. 6, London, Oxford Medical Publications, 1942, p. 1399.

2. Crocker, H. R.: Diseases of the Skin: Their Description, Diagnosis and Treatment, ed. 3, London, H. K. Lewis, 1903.

3. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, London, Henry Kimpton, 1939, p. 567.

4. Ronchese, F.: Ichthyosiform Atrophy of the Skin in Hodgkin's Disease, Arch. Dermat. & Syph. **47**:778 (June) 1943.

5. Glazebrook, A. J., and Tomaszewski, W.: Ichthyosiform Atrophy of the Skin in Hodgkin's Disease, Arch. Dermat. & Syph. **50**:85 (Aug.) 1944.

start of the ichthyosiform changes, which developed within nine weeks. Besides the presence of jaundice, evidence of a sick liver was afforded by tests of impairment of hepatic function. Loss of eyebrows and eyelashes was a feature, with falling of the scalp hair, and hyperkeratosis was greatest on the soles.

Histologically, the skin showed a picture of atrophy and hyperkeratosis, reported by the pathologist as being suggestive of a vitamin deficiency.

A striking diminution of the plasma content of vitamin A and of carotene was found in this man, together with a pathologic excretion of vitamin A in the urine. Treatment with vitamin A was tried, but its effects were masked by the fluctuating but progressive nature of the

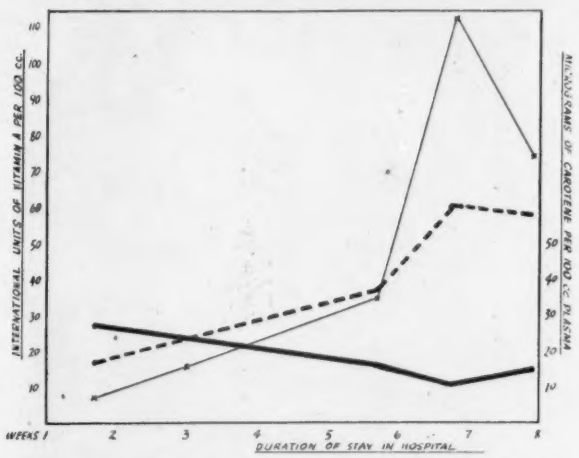

Fig. 1.—Variations in the concentrations of plasma vitamin A are shown by the interrupted line and of urinary vitamin A by the fine line. In both cases the measurement has been recorded in international units per hundred cubic centimeters. The thick black line shows the level of plasma carotene, in micrograms per hundred cubic centimeters. From the commencement of the second week of his illness, the patient received every day 72,000 international units of vitamin A by mouth, and 100,000 international units of vitamin A by injection.

illness. It was not possible to obtain a postmortem examination. Soon afterward, a patient with similar skin changes was admitted to the ward.

REFORT OF A CASE OF ICHTHYOSIFORM ATROPHY OF THE SKIN IN SARCOMA

A casual laborer aged 44 came to the hospital complaining of the effects of a swelling in the right arm pit. He told us that he had been unduly pigmented for about five years. His was an outdoor occupation, and he ascribed the pigmentation to sunburn, although it affected parts of his body normally covered.

He had noticed a painless lump in the right arm pit three months before admission, together with a weak feeling and short attacks of fever. At this

time, the skin of his hands became dry and scaly, and a little later the skin of his trunk was similarly affected.

Biopsy of the right axillary gland was carried out the following month. It was found to be neoplastic, and arrangements were made to admit the patient to the hospital for high voltage roentgen therapy, but owing to a shortage of beds this could not be done until another month had elapsed. After the operation, he began to lose weight a little. The scaliness of his skin persisted. His diet had been adequate, and there was no sugggestion of night blindness.

Examination on Admission to Hospital.—His general nutrition was fair. There was a diffuse brown pigmentation of the entire body, having the distribution and appearance of melanin, but the mucosae were spared. The skin was everywhere dry and atrophic, with a tendency to hyperkeratosis on the soles, but it showed no evidence of any infiltration or inflammation, while the surfaces of the nails were uneven and transversely ridged.

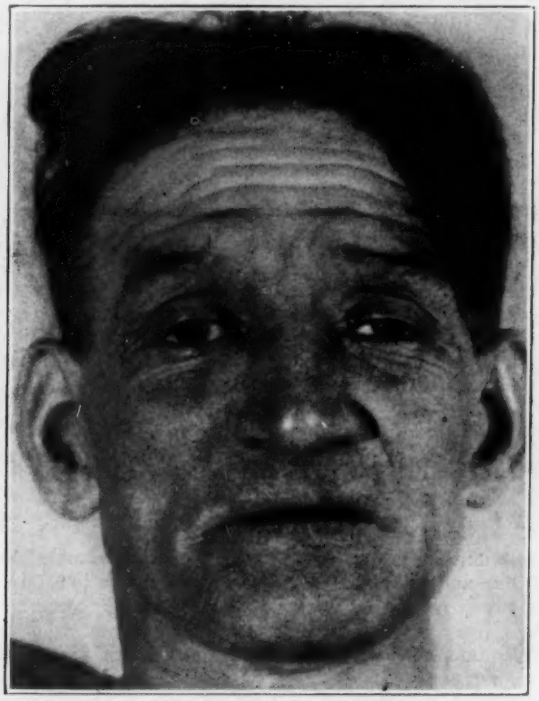

Fig. 2.—Note the entire loss of eyelashes, the partial loss of the eyebrows, the scaliness of the skin of the face, the cheilosis and the scaliness of the lips, the scaliness of the scalp and the falling of the hair.

On the forehead, around the eyes and the mouth and at the base of the neck, the skin was scaly and keratinized coming off in white flakes of 3 to 4 mm. in diameter. There were fissured cracks at the corners of the mouth.

His dark hair showed early graying, and was straight and unhealthy looking, the patient complaining that it had been falling recently. Eyebrows and eyelashes were still present.

The mouth was clean, the tongue red, moist and smooth and atrophic. No pathologic changes were seen in the tonsils. There were a few small painless lymph nodes in the left axilla, both groins, both posterior triangles and the left occipital region.

The liver was firm, large and smooth, being palpable 3 inches (7.6 cm.) below the costal margin. At times, it was tender to touch. The spleen was not felt.

Tests of Hepatic Function.—During the first week of hospital treatment the icterus index was 3, and there was no excess of urobilinogen in the urine. After a test dose of 6 Gm. of benzoic acid the total excretion in the urine of hippuric acid was 2 Gm. for a period of four hours. There was 2.25 Gm. of albumin per hundred cubic centimeters of blood, and 4 Gm. of globulin. The albumin-globulin ratio was reversed. The plasma phosphatase was 195 units (determined by the modified Kay method).

During the sixth hospital week, when there was some improvement in the eruption, there was 1.88 Gm. of albumin per hundred cubic centimeters, 2.83 Gm. of globulin and 115 units of plasma phosphatase.

Fig. 3.—The skin of the abdomen. Note the scaliness and pigmentation.

The patient was too weak for other tests to be made. Together, the results show that the hepatic function was impaired.

Estimations of Vitamin A.—The results have been charted (fig. 1).

Low levels of plasma vitamin A were found, and in spite of an intake of 172,000 units per day, partly by mouth and partly parenterally, at no time did the plasma vitamin A reach even the low normal level of 70 international units per hundred cubic centimeters.

The plasma carotene concentration was below normal to begin with, and fell even lower after treatment with vitamin A. In the previous case which we reported [5] the carotene value rose after vitamin A therapy.

Vitamin A, as was determined by the Carr-Price reaction, was excreted in the urine throughout the illness, the excretion increasing as the disease progressed, so that eventually there was a higher concentration of vitamin A in the urine than in the blood. We have no explanation to offer for this phenomenon.

Examination of the Blood.—A blood count showed a hemoglobin concentration of 67 per cent, 4,600,000 red cells and 13,200 white blood cells, of which 85 per cent were polymorphonuclear leukocytes, 6 per cent monocytes, 7 per cent lymphocytes, 1 per cent eosinophils and 1 per cent basophils.

The anemia steadily progressed throughout the illness, and just before the patient's death the red cell count had fallen to 1,700,000, the white cell count to 1,800 and the hemoglobin concentration to 30 per cent.

Course—On admission, pyrexia developed, and it persisted for five days. After an interval of five days, a second period commenced, which terminated just before his death on the forty-eighth hospital day.

The skin deteriorated at first, becoming everywhere drier and more scaly, and flaking off his body in sheets. The skin of the hands cracked and oozed serum. A purulent conjunctivitis appeared, with a tendency to ectropion, and the eyelashes

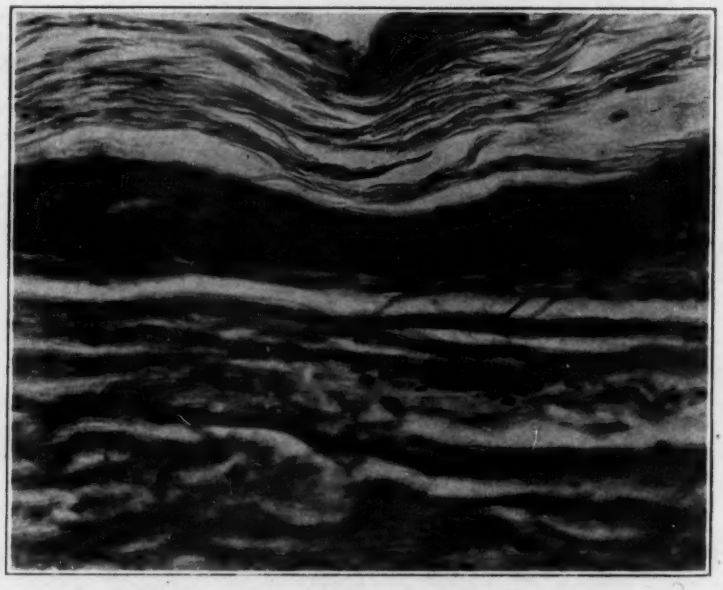

Fig. 4.—Section of skin showing atrophy and hyperkeratosis.

were lost, but there was no further falling of the thin scalp hair or the eyebrows (fig. 2).

During the sixth week, a definite improvement was observed in the skin, which became softer and less flaky. The eyes improved with simple lotions. This improvement coincided with a fall in the temperature and a rise in the plasma vitamin A concentration to 50 international units per hundred cubic centimeters.

The patient's general condition was poor, however, and thereafter he went quickly downhill, dying on the forty-eighth day after admission. During his last week, the cutaneous pigmentation increased greatly over his abdomen (fig. 3).

Postmortem Examination.—A mass of firm fleshy glands extended from the supraclavicular region down into the thorax along the line of the trachea, through the diaphragm into the abdomen around the aorta. There was also a large mass of glands in the mesentery and in the lesser omentum.

The firm fatty liver was enlarged and weighed 1,900 Gm. It contained no secondary deposits.

The spleen and the suprarenals showed congestive changes.

Histologic Findings.—Glands: The normal cell architecture was replaced by a spindle cell sarcoma.

Liver: The parenchyma showed pronounced fatty degeneration, with areas of focal necrosis.

Skin: The epidermis was definitely atrophic, and in some places was only a few cells thick. It was covered with a moderate amount of keratin. There was an increase in the amount of melanin in the basal cells in some regions. The appearances were suggestive of a vitamin deficiency (fig. 4).

Diagnosis.—The diagnosis was spindle cell sarcoma involving the lymph glands. The primary growth was not found. There was fatty degeneration and focal necrosis of the liver and atrophy of the skin suggestive of a vitamin deficiency.

COMMENT

It is of interest, at this point, to consider the theories which have been advanced to explain the skin changes in acquired ichthyosis. It has been thought that hypothyroidism and various toxic conditions, particularly such as affect the nervous system, possibly play a part in the pathogenesis of the acquired disease. Localized ichthyotic development may occur in connection with neuritis from injury or disease, but there seems to be no evidence to implicate the nervous system as a causal factor in the generalized type.

The evidence for hypothyroidism is the fact that these patients sometimes have a reduced basal metabolic rate. Often, however, the metabolic rate is normal. The skin shows no resemblance to that found in hypothyroidism, and thyroid extract does not improve the condition. The Suttons [3] stated that thyroid medication frequently makes patients with true ichthyosis more agitated and pruritic.

Diasio [6] pointed out that the formation of keratin is a specific function of the epithelial cells. He stated his belief that ichthyosis, an example of the dry type of dyskeratosis, is characterized by premature keratinization due to premature aging of the prickle cells. Could a nutritional upset account for this faulty aging process?

During recent years, great interest has been taken in the dermatoses associated with vitamin A deficiency, particularly a disorder sometimes termed "phrynoderma" or toad skin. Rapaport, Herman and Lehman [7] discussed the considerations linking ichthyosis with vitamin A deficiency.

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6. Diasio, F. A.: Paronychia Congenita, Jadassohn, Arch. Dermat. & Syph. **30**:218 (Aug.) 1934.

7. Rapaport, H. G.; Herman, H., and Lehman, E.: Treatment of Ichthyosis with Vitamin A, J. Pediat. **21**:733 (Dec.) 1942; correction, ibid. **22**:120 (Jan.) 1943.

First of all, they pointed out that in both diseases there is often a seasonal influence, with great amelioration during the summer, and they suggested that the frequent delay in the appearance of ichthyosis until after weaning is in favor of a dietary factor in its causation.

In both phrynoderma and ichthyosis there is a decided dryness of the skin, and in both diseases there is a predilection for the involvement of the extensor surfaces, with sparing of the flexor folds.

Phrynoderma is characterized by the keratotic plugs which protrude from the hair follicles; these lesions are usually indistinguishable from those termed "keratosis pilaris," which are sometimes present in cases of ichthyosis. The illustrations of phrynoderma published by Radhakrishna Rao [8] are strikingly similar to cases of ichthyosis.

There are also pathologic similarities. In both disorders there is a hyperkeratinization with excessive proliferation and cornification of the horny layer of skin. Phrynoderma, however, involves more particularly the hair follicles, while ichthyosis tends to involve the skin between the follicles.

If there is any connection between vitamin A deficiency and ichthyosis, it cannot be said of the majority of patients that their dietary intake is inadequate, although the acquired ichthyosis arising in users of Piper methysticum might well be due to malnutrition. Natives addicted to this drug spend all their time obtaining it and neglect their nutritional needs. In other cases, vitamin A deficiency might arise in the tissues by malabsorption or some metabolic defect.

Peck and his co-workers have reported disturbances in vitamin A metabolism in Darier's disease. Peck, Glick and Chargin [9] found abnormally low levels of vitamin A in the blood of 2 patients with congenital ichthyosis, although dark adaptation studies in the same cases showed the patients to be normal in this respect.

How does vitamin A therapy affect the dyskeratoses? Substitution therapy did not cure the 2 patients with congenital ichthyosis reported by Peck, but he and his colleagues obtained improvement in nearly all their patients with Darier's disease who were treated with large oral doses of vitamin A, amounting to 200,000 U. S. P. units per day. Rapaport, Herman and Lehman [7] noted an improvement in the skin of 6 patients with ichthyosis after prolonged treatment with vitamin A —200,000 international units daily for one year in 1 case—and they stated their belief that some hereditary disorder of vitamin A metabolism may be the basis of ichthyosis. Cod liver oil has been used

8. Radhakrishna Rao, M. V.: Studies on Vitamin A Deficiency: Histopathology of the Skin in Human Keratomalacia, Indian J. M. Research **25**:39 (July) 1937.

9. Peck, S. M.; Glick, A. W., and Chargin, L.: Vitamin A Studies in Cases of Ichthyosis, Arch. Dermat. & Syph. **48**:32 (July) 1943.

empirically in the treatment of ichthyosis for many years, and other investigators have recorded an improvement in ichthyosis following vitamin A therapy.[10]

The skin changes in the cases of Hodgkin's disease described by Ronchese [4] and ourselves [5] might truly be described, from their appearance to the naked eye, as an ichthyosis, although Ronchese has coined the name "ichthyosiform atrophy" for the syndrome.

In the case described herein, there was a striking similarity in the cutaneous manifestations to those in our case of Hodgkin's disease which we have mentioned. Atrophy, however, was more pronounced a feature of the former, while hyperkeratosis marked the latter. The histologic appearances were similar in the two cases, and resembled, according to the pathologist, a vitamin deficiency.

Why should such a similar cutaneous lesion develop during the course of two illnesses, each the result of an entirely different underlying disease process? In neither was this cutaneous disturbance due to cellular infiltration into the skin, and some functional upset, common to both diseases, must be looked for. The most obvious link between the two conditions was a severe disturbance of hepatic function, revealed by laboratory tests, although there were clinical indications of a sick liver in each case—jaundice in the one, and an enlarged and tender liver in the other. We do not know the nature of the pathologic lesion in the first, but the liver of the second patient was the seat of fatty change and focal necrosis.

It is known that hepatic dysfunction may result in upsets in vitamin A metabolism, and severe disturbances of vitamin A metabolism were present in both cases, manifested by abnormally low levels of plasma vitamin A and of carotene, and by the pathologic excretion, according to the Carr-Price reaction, of vitamin A in the urine. The results of treatment with large doses of vitamin A were not impressive. But the basic disease process in both cases was malignantly progressive, and vitamin A therapy failed to restore the plasma concentration in the second case even to a low normal level. It is not to be expected, therefore, that substitution therapy could be successful under such circumstances.

The abnormal vitamin A findings in these 2 men afford a possible connecting link between the condition of their skin and that found in other cases of ichthyosis. The responsible mechanism may not always

10. Baer, H. L., and Vogel, H. R.: The Biophotometric Study of Vitamin A in Dermatological Conditions, Urol. & Cutan. Rev. **44**:176 (March) 1940. Vail, D.: Corneal Involvement in Congenital Ichthyosis (Keratoderma), Arch. Ophth. **24**:215 (July) 1940. Wise, F., and Sulzberger, M. B.: The 1938 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1939, p. 282.

be of the same nature. We should like to mention, however, that the liver in our case of sarcoma was found after death to contain approximately 3,000,000 international units of vitamin A, an abnormally high amount. Also, fluorescent microscopy revealed a disturbance in the distribution of vitamin A in the tissue of the liver. These observations suggest that, as the plasma vitamin A concentration persisted at such a low level, the liver must have been holding back vitamin A from the blood stream. Such an explanation does not afford any indication, however, as to why vitamin A was excreted in the urine in both cases.

SUMMARY

A case of lymphosarcoma with ichthyosiform atrophy of the skin has been described. Hepatic damage, with evidence of abnormal metabolism of vitamin A, was found.

OCULAR PEMPHIGUS WITH SCARRING OF THE SKIN AND MUCOUS MEMBRANES

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VANCOUVER, BRITISH COLUMBIA, CANADA

PEMPHIGUS of the conjunctiva is a rare variety of pemphigus. In a comprehensive, statistical analysis of pemphigus, Lever and Talbott [1] found it to occur in about 16 per cent of cases. Although ocular pemphigus always results in scarring, the concomitant involvement of other mucous membranes, such as the buccal mucosa, esophagus, pharynx, penis and vulva, is not as a rule found. Lever,[2] in a review

Fig. 1.—Symblepharon of the right eye and the dry, scaly, clouded right cornea.

of the literature, was able to find only 5 cases of scarring of the skin and reported 6 additional cases. The following case is deemed worthy of reporting, since there is the clinical picture of ocular pemphigus, with scarring of both the skin and the mucous membranes.

1. Lever, W. F., and Talbott, J. H.: Pemphigus, Arch. Dermat. & Syph. **46**:348 (Sept.) 1942.

2. Lever, W. F.: Pemphigus Conjunctivae with Scarring of the Skin, Arch. Dermat. & Syph. **46**:875 (Dec.) 1942; Pemphigus Conjunctivae with Scarring of the Skin, ibid. **49**:113 (Feb.) 1944.

REPORT OF A CASE

History.—C. G., a Scottish born white man aged 63, was first seen on Oct. 7, 1944. He was complaining of "trouble" with his right eye and recurring blisters on the glans penis of seven years' duration, blisters in the mouth, nose and throat off and on for the past five years and "sores" on the tip of his nose during the past two years.

There was a past history of injury to his right eye twelve years before, which was treated with successful results by an ophthalmologist. Then four years later, he had herpes zoster on the left side of his chest, of six weeks' duration

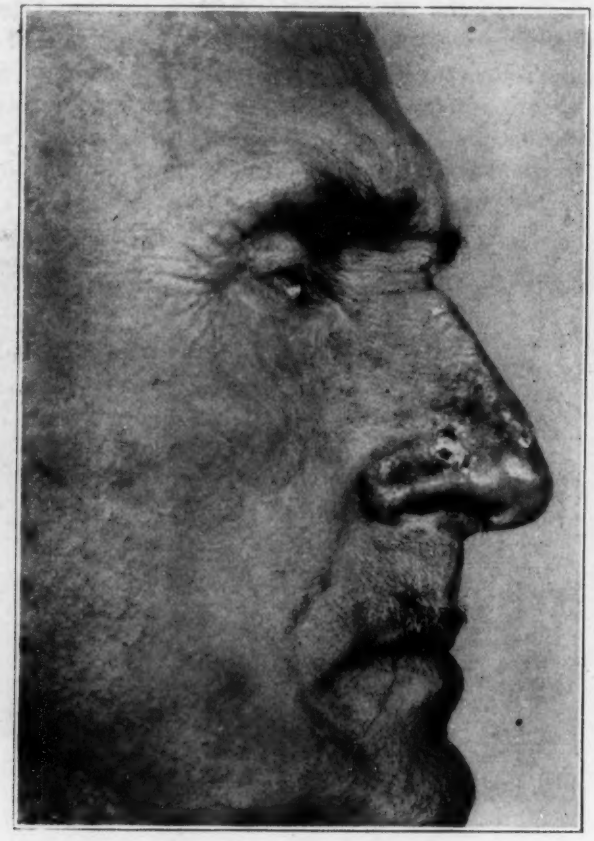

Fig. 2.—Lateral view of the nose, revealing superficial scarring and adherent crusts.

and he claims that he has not felt well since. In the intervening eight years his weight has dropped from 161 to 135 pounds (73 to 61.2 Kg.).

Present Illness.—About seven years ago the right eye became "sore," and the eyelashes would point inward and rub the eyeball, necessitating medical attention. Coincident with this, blisters developed on the glans penis, recurring with adhesions and scar formation. For the past five years he had been aware of recurring attacks of blisters on the buccal mucosa on the right side, soft palate, pharynx

and inside his nose; the lesions would break quickly and heal in two to seven days. These were at times painful, and when nervous and excited the patient would experience dysphagia. During the past two years "sores" and blisters have also recurred on the distal end of his nose. A plastic operation was performed on the right lower lid in another city about two years before he was seen. The result was not good, due to rapid formation of scar tissue.

Examination.—The patient is asthenic and in no apparent distress.

Skin and Mucous Membrane.—1. Head and Neck: The scalp shows thinning of the hair, with seborrheic alopecia of the vertex region.

2. Eyes: The report of the ophthalmologic examination by Dr. John A. McLean is as follows: In the right eye there is light perception. The globe is somewhat shrunken, and tension is low. The upper and lower cul-de-sacs are completely obliterated except for a small sinus under the upper lid, which discharges purulent material. The cornea is dry, white and opaque and covered

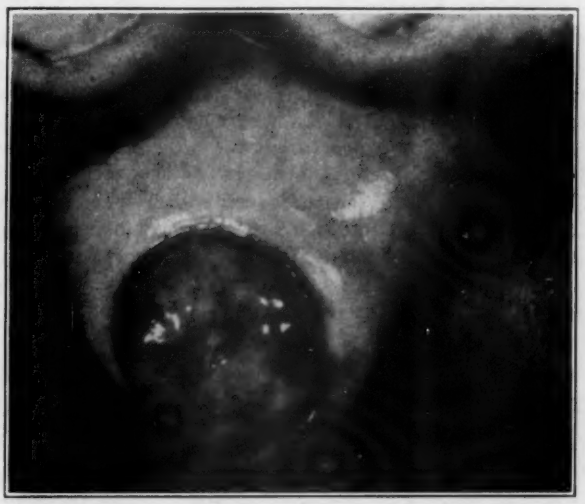

Fig. 3.—Scarring of the glans penis and the extent of retraction of the foreskin.

with a thick, dry crust, which one is unable to remove with forceps. In the left eye the vision is 20/20 and the cornea, iris, lens and fundus are normal.

3. Mouth: The patient wears upper and lower dentures. The tongue and lips are normal. On the right buccal mucosa, along the denture line, there is a fine, white, lacy scar, and proximal to this there is a small flaccid bulla. There are aphthous-like lesions, but larger, on the soft palate and the pharynx. The mucous membrane of the posterior pharyngeal wall has a dry, glazed appearance. There is no evidence of tonsillar tissue, although the patient denies ever having had a tonsillectomy. The posterior tonsillar pillars are adherent to the posterior lateral pharyngeal wall. The nasopharynx is definitely stenosed and scarred. The eustachian tube cushions are adherent to the soft palate, and there is almost complete obliteration of the fossae of Rosenmüller. The mucous membrane of the nose is dry and shows a decided degree of atrophy. On the distal end of the nose there are small, scattered, adherent, dry crusts, situated at the periphery

of an area of fine, cigaret paper type of scarring. This area is erythematous in color.

4. Left Side of the Chest: On the anteroposterior surface there is post-herpes-zoster scarring and depigmentation.

5. Penis: There are adhesions between the foreskin and the glans penis, preventing retraction of the foreskin. The glans penis has a moist, velvety, violaceous appearance, and there is an atrophic scar about the meatus.

The rest of the cutaneous surface is normal in appearance.

Results of the physical examination were essentially within normal limits; the pulse rate was 88, and the blood pressure was 140 systolic and 90 diastolic.

Laboratory Data: The result of the examination of the blood was as follows: hemoglobin content 88 per cent, red blood cells, 4,430,000 per cubic millimeter, white blood cells, 9,000 per cubic millimeter, polymorphonuclear neutrophils 63 per cent, polymorphonuclear basophils 1 per cent, polymorphonuclear eosinophils 4 per cent, lymphocytes 26 per cent and monocytes 6 per cent. The Wassermann reaction of the blood was negative.

Subsequent Course.—The patient was again seen on July 16, 1945, and there were new bullae present on his nose and on the right buccal mucosa. Punch biopsies of these two areas were attempted but were unsuccessful, as the bullae separated from the affected areas. Treatment to date has consisted of electrolysis for the trichiasis and administration of various vitamin preparations, including riboflavin. On empiric grounds, the patient was given a course of weekly intramuscular injections of 1 cc. of bismuth subsalicylate. He was last seen on September 12 and at that time he stated that he had gained 5 pounds (2.3 Kg.) and felt better. However, examination revealed some scarring of the lower cul-de-sac in the left eye, with beginning symblepharon, and new bullae on the nose and buccal mucosa. Also, there is further limitation in the ability to retract the foreskin, due to adhesions.

COMMENT

According to Rycroft,[3] ocular pemphigus was first described as far back as 1858 by White Cooper as conjunctival xerosis, and it was not until 1879 that von Graefe identified pemphigus with what had been called "essential shrinking of the conjunctiva." The incidence of pemphigus of the conjunctiva to other eye diseases is about 1 to 20,000. The disease is resistant to all treatment and leads to the inevitable end result of blindness after the patient has passed through the stages of vesiculation, cicatrization and, finally, the stage of complications. Vesicles vary in size from that of peas to that of beans and are seen in about 12 per cent of cases on either the palpebral or the bulbar conjunctiva, the site of election being at the inner canthus and at the center of the lower conjunctival fornix. Corneal involvement is always secondary. This is followed by the appearance of firm bands of fibrous tissue, which eventually obliterate the fornices and impair the mobility of the globe. Later, the eyelids and globe become firmly adherent in a mass of pericorneal adhesions, which strangle the orifices of the lacrimal ducts and produce xerosis of the conjunctiva. Ankyloblepharon is

3. Rycroft, B. W.: Ocular Pemphigus, Brit. J. Ophth. **18**:571 (Oct.) 1934.

almost constant. Finally, a coarse pannus and fibrous tissue invade the cornea. Trichiasis and entropion may give rise to traumatic corneal ulcers, which can lead to suppurative panophthalmitis.

Other mucous membranes involved are those of the nose, throat, mouth, esophagus, vagina and penis, which as a rule do not heal with scarring, in contradistinction to the inevitable result in ocular involvement. Mastication and swallowing are never sufficiently painful to prevent an adequate intake of food. The vermilion border of the lips, to which the oral lesions of pemphigus vulgaris often spread, is never involved. Cutaneous lesions are always limited to a few areas, and the general health is but little affected.

Pemphigus of the conjunctiva is a chronic and benign disease. In the reported cases, it was found to be commoner in the female sex, with the average age of onset between 45 and 70 and the average duration of the disease seven to eight years. The average eosinophil count is 3.3 per cent. None of the patients were Jewish, in contrast to the incidence of 33⅓ per cent in pemphigus vulgaris, pemphigus foliaceus and pemphigus vegetans, which are debilitating and often rapidly fatal diseases. Involvement of the eyes is seen only in acute pemphigus and ocular pemphigus.

The differential diagnoses entertained in the present case were (1) drug eruption, (2) Behcet syndrome, (3) erythema multiforme bullosum and (4) dermatitis herpetiformis. However, the clinical picture in combination with the patient's age, race and general good health and duration of the disease fulfils all the criteria noted in the careful clinical analysis of cases reported by Lever and Talbott.[1]

CONCLUSIONS

1. A case of ocular pemphigus is reported, the condition occurring in a Scottish born man showing characteristic lesions. Although the disease is apparently chronic and benign, it is leading to the inevitable end result of scarring and blindness.

2. This case is an example of ocular pemphigus with scarring of both skin and mucous membranes.

Dr. John A. McLean granted permission to report this case, and Mr. John B. Edwards, of the X-Ray Department of the Vancouver General Hospital, supplied the illustrations.

606-607 Birks Building.

LIPOIDOSIS CUTIS ET MUCOSAE

Report of a Case

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MEDICAL CORPS, ARMY OF THE UNITED STATES

LIPOIDOSIS cutis et mucosae has been reported so infrequently as to be considered a rare disease. However, sufficient cases [1] have been presented in the literature so that it emerges as a well defined clinical entity with a pathognomonic histopathologic picture. According to Urbach,[2] the disease is characterized by abnormal deposits of lipids in the skin, mucous membranes and possibly also in other tissues. From histochemical studies employing differential staining procedures and solubilities in various organic solvents, Urbach came to the conclusion that the lipid was of the group of acetone-soluble phosphatides and that it was combined with protein in a physical adsorptive union. Therefore, he suggested the name lipoid proteinosis for this disease.[3] In support of this concept, Montgomery and Havens [4] and J. Ramos e Silva [5] were able to show a decided increase in the phospholipid content of lesions which were subjected to chemical analysis. However, others —Wile and Snow [6] and Hansen [7]—found no such increase.

From the Dermatology Section of the Medical Service of Battey General Hospital, Rome, Ga.

1. Campbell, A. D.: Lipoid Proteinosis (Urbach-Wiethe), U. S. Nav. M. Bull. **42**:669 (March) 1944. Campbell's report makes a total of 31 cases published.

2. Urbach, E.: Beiträge zu einer physiologischen und pathologischen Chemie der Haut; über eine familiäre Lipoidose der Haut und der Schleimhäute auf Grundlage einer diabetischen Stoffwechselstörung, Arch. f. Dermat. u. Syph. **157**:451, 1929.

3. Urbach, E.: Lipoidproteinose (Lipoidosis cutis et mucosae), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 2, pp. 335-352.

4. Montgomery, H., and Havens, F. Z.: Xanthomatosis: IV. Lipoid Proteinosis (Phosphatide Lipoidosis), Arch. Otolaryng. **29**:650 (April) 1939.

5. Ramos e Silva, J.: Lipoid Proteinosis (Urbach-Wiethe), Arch. Dermat. & Syph. **47**:301 (March) 1943.

6. Wile, U. J., and Snow, J. J.: Lipoid Proteinosis, Arch. Dermat. & Syph. **43**:134 (Jan.) 1941.

(Footnotes continued on next page)

In discussing a paper of Wise and Rein,[8] Montgomery stated in part:

> Further investigation is necessary before dermatologists can be sure that chemically the condition is a disturbance in phosphatide-lecithin metabolism. In the study of future cases I should like to urge observers to make quantitative chemical analyses of the diseased skin for the various lipoids, rather than to depend on different tinctorial staining reactions to distinguish, for instance, between cholesterol, phosphatides and the fatty acids.

Recently a patient with lipoidosis cutis et mucosae came under our observation, and we were able to obtain comparatively large specimens of diseased skin for chemical analysis. The purpose of this paper is to report another case of this disease and to present the results of our chemical studies.

During the past decade, the syndrome has been described in detail in the American literature. Most of the patients in the reported cases have so many signs and symptoms in common that the well developed condition should be recognized readily. The following report presents a fairly typical case.

REPORT OF A CASE

S. H., a 22 year old white soldier, Jewish, born in the United States, was admitted to the Dermatology Section in March 1945, having been transferred from an overseas hospital, where he had been under observation for lesions of the skin and oral mucous membranes. He had been hospitalized because a dental officer, on noting the lesions in the mouth, had requested observation for syphilis. While in the hospital there he developed a pruritic eruption, which was diagnosed as scabies. Shortly after recovery from this eruption (sulfur ointment had been used in treatment), there developed, for the first time in his life, pea-sized to nickel-sized discrete blebs on the hands, elbows, buttocks, thighs and left sole. These blebs gradually became covered with yellowish crusts and slowly went on to healing. When he was examined by one of us (H.P.) three months after the onset of the bullous eruption, he showed residual patches consisting of erythema, purplish brown pigment and atrophy. A few areas retained an impetiginous-like crust overlying superficial, healing, clean ulcers.

Family History.—His father and mother were third cousins. He has one brother and three sisters, all of whom are in good health. One of his sisters, however, has similar cutaneous and mucosal lesions but to a lesser degree. She, like the patient, has been hoarse from infancy and has sparse scalp hair. To his knowledge, no relative has ever had diabetes.

Personal History.—He was apparently a normal baby at birth, but early during infancy hoarseness was noted. His skin was clear until about the age of 1, when an eruption appeared on the face, neck and ears, which was vaguely described as consisting of redness and crusting. The family physician called the eruption "teething eczema," and it lasted for an unknown period, "until my teeth came out."

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7. Hansen, P.: Ein Fall von Lipoidproteinose, Arch. f. Dermat. u. Syph. **175**:618, 1937.

8. Wise, F., and Rein, C. R.: Lipoidosis Cutis et Mucosae (Lipoid Proteinosis of Urbach), Arch. Dermat. & Syph. **37**:201 (Feb.) 1938.

After the eruption subsided, the face was left with "enlarged pores." As far back as he can remember, he has been aware of a feeling of roughness in the mouth, of dry chapped lips and of a thick tongue, which could not be protruded normally.

In 1927, at the age of 4, because of progressive huskiness of the voice, he was hospitalized, but "no evidence of laryngeal disease was found." From 1932 to 1934, he had recurrent swellings of the parotid glands, for which he was seen by a surgeon, who "drained the right cheek by division of Stenson's duct in the mouth." After this procedure the swellings subsided, and they recurred no more.

At the age of 12, he first noticed red lesions on the elbows and along the extensor surfaces of the forearms. The lesions on the elbows became warty, and he remembers that frequently he would induce bleeding by picking. The color of the eruption gradually faded, and the lesions flattened out somewhat. He was unaware of other lesions on the body until the examiner pointed out other areas involved.

For the past few years he had noticed a progressive thinning of the scalp hair. No other symptoms were elicited.

He had suffered no disability from his disease and in 1943 was inducted into the Army, in which he had no difficulty with routine training.

Physical Examination.—The patient was a well developed white man, who appeared older than his actual age of 22. The voice was hoarse. General examination revealed no significant findings other than the changes in the skin, mucous membranes and teeth. These abnormalities were for the most part strikingly symmetric.

Skin: The face, ears and scalp had a faint yellowish hue. There was diffuse thinning of the scalp hair, with a tendency to premature baldness extending backward from the forehead. The face presented somewhat of a pock-marked appearance, which on close inspection was found due to an admixture of varioliform depressions and barely elevated, smooth, irregular infiltrations. On the forehead, wrinkling was pronounced and the skin appeared thickened.

Along the edges of the upper eyelids there was a row of closely set, pinhead-sized to matchhead-sized, flesh-colored nodules. The cilia penetrated through these masses, resulting in considerable displacement in the normal arrangement of the lashes. The lower lids showed only a few discrete papillary excrescences. A prominent finding was the noticeable enlargement of all four lacrimal papillae, which measured up to 5 mm. in height. The lacrimal openings, which ordinarily are ellipsoidal, had assumed a circular configuration. No obstruction to tear drainage was noted.

In the axillas, the cutaneous folds were thickened and formed parallel pinkish tan ridges. The rest of the axillary skin had a light tannish color, due in part to pinhead-sized, rounded, closely set papules. A similar type of lesion involved the nates. On the opposed surfaces of the buttocks, crescentrically arranged, there were nodular pinkish tan plaques with roughened hyperkeratotic surfaces.

Over the point of each elbow there were quarter-sized hyperkeratotic, warty, brownish pink, elevated, elastic plaques, which were surrounded by a halo of pinkish tan thickened skin. Continuing downward along the ulnar aspect of the forearms to the lower third, there were light tan triangular patches of thickened skin, in which accentuated cutaneous lines formed flat polygonal papules, giving at first glance the appearance somewhat of circumscribed neurodermatitis.

Over the dorsolateral aspect of a number of the fingers there were a few confluent, rough, flesh-colored papules.

Extending upward from the level of the fourth lumbar vertebra in the midline there was a 3 by 12 cm., flesh-colored, thickened plaque, in which the cutaneous lines and follicular openings were prominent.

The remains of the bullous, crusted lesions which the patient described were seen as discrete nummular patches on the dorsum of the hands and fingers and on the left elbow, buttocks and thighs. Some of the younger lesions still retained a dry, brownish crust. The older lesions were erythematous, with varying degrees of pigment, suggesting fading purpura. A few patches showed atrophic depressions.

Mucous Membranes: The lower lip was thickened, dry and everted and had parallel vertical fissures. The upper lip was involved to a lesser extent. On the inner surfaces of the lips there were multiple, elevated, firm, whitish yellow nodules of a size up to that of a split pea, some discrete but for the most part coalescent, thus producing a cobblestone-like appearance (fig. 1). Similar infil-

Fig. 1.—Nodules on the lower lip and under surface of the tongue. Note retention of the lower central incisors.

trations involved the mucosa of the upper buccal region, the faucial pillars, the tonsillar beds and the posterior pharyngeal wall. The papillae about the openings of the parotid ducts were considerably enlarged and prominent. The right parotid duct was scarred. The gingiva showed no abnormalities, and no ulcerations were noted. There was a pale yellowish cast to the tongue and palate. The tongue was smooth but appeared thicker and larger than normal and had a firm "woody" feel. It could not be protruded beyond the lips, for it was checked and pulled down by the greatly thickened and shortened inelastic frenum, which, with the under surface of the tongue, showed the characteristic nodulations. The vocal cords were involved by a similar process and appeared paler than normal. Abduction and adduction were performed satisfactorily, but the edges were roughened and uneven.

Teeth: Roentgenologic and dental examinations revealed congenital absence of the upper lateral incisors, lower central incisors and second bicuspids. The lower deciduous central incisors were still retained (fig. 2). A single transverse striation involved each of the crowns of the upper central incisors, upper cuspids, lower lateral incisors and lower cuspids, above which the teeth were hypoplastic.

Laboratory Studies.—Roentgen examination of the skull, long bones, pelvis and ribs showed no abnormalities; the heart and lungs appeared normal, and no enlargement of the spleen or liver was visualized. The electrocardiogram was normal. The hematocrit reading, sedimentation rate, white cell count and differential counts were within normal limits. The Kahn reaction was negative. The basal metabolic rate on two occasions was —10 per cent. The oral and intravenous glucose tolerance tests gave normal values. The sulfobromophthalein test for hepatic function on three occasions showed retention of 6 per cent, 2.5 per cent and 5 per cent of the dye.[9] Other tests of hepatic function, however, including galactose tolerance, cephalin flocculation, hippuric acid synthesis and icterus index gave no evidence of hepatic disease. The examination of the urine presented no abnormalities. Analysis of the lipid components of the blood serum gave values within normal limits.

Chemical Analysis of Tissue.—The warty plaque on each elbow was surgically removed and subjected to chemical analysis for total lipid, cholesterol and phospholipid content. Specimens of normal skin, which were obtained for us by the surgical service, were also analyzed in order to give us control values. The technic employed was as follows: The excised skin was trimmed of all subcutaneous fat, weighed and frozen. It was then dried in a desiccator under high vacuum. When the weight was constant the tissue was cut into small pieces, placed in a Soxhlet extractor and extracted with alcohol-ether mixture for twenty-four hours. The alcohol-ether was evaporated off and the residue extracted several times with petroleum-ether. This extract was then collected in a tared flask, the ether evaporated off and the residue dried to constant weight. To be certain that all lipid material had been removed from the previously extracted tissue, it was dissolved in 10 per cent sodium hydroxide solution and, after acidification with sulfuric acid, extracted with several portions of petroleum-ether. The petroleum-ether extracts were added to the flask containing the first residue and evaporated off. The flask was again brought to constant weight and the weight

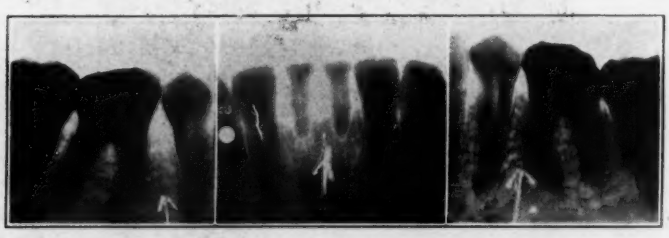

Fig. 2.—Roentgenograms of the teeth, showing congenital absence of the lower second bicuspids and permanent lower central incisors. The deciduous lower incisors are still retained.

9. A dosage of 5 mg. per kilogram of body weight is employed, and the specimen for analysis is obtained forty-five minutes after injection of the dye. Any retention is considered abnormal.

of the residue noted. In this manner it was found that an additional amount of lipid was recovered, usually less than 5 per cent of the total lipid. The fatty material was dissolved in an appropriate volume of alcohol-ether, and aliquots were then removed for the estimation of cholesterol and organic phosphorus levels.

TABLE 1.—*Comparative Results of Chemical Analyses of Diseased Tissues* *

	Our Results		Wile and Snow [6]				
	First Specimen	Second Specimen †	First Specimen	Second Specimen	Montgomery and Havens [4]	Hansen [7]	Ramos e Silva [5]
Weight of wet tissue.....	4.36 Gm.	5.12 Gm.	210 mg.	307 mg.	840 mg.	.....	116 mg.
Weight of:							
Total lipids.....	64 mg.	33 mg.	12.20 mg.	10.70 mg.			
Cholesterol.....	12 mg.	6 mg.	1.65 mg.				
Phospholipids.....	4 mg.	1.20 mg.	.....	0.73 mg.	.....	.....	8.20 mg.
Per cent of wet tissue:							
Total lipids.....	1.47	0.64	5.80	3.50	1.9‡	1.56	
Cholesterol.....	0.27	0.12	0.78	....	0.3		
Phospholipids.....	0.09	0.02	....	0.24	1.5	0.338	7.06
Per cent of total lipids:							
Cholesterol.....	18.70	18.20	13.50	.....	16		
Phospholipids.....	6.25	3.60	.....	6.80	79		

* The chemical determinations were done by First Lieutenant William V. LaRosa, of the chemistry laboratory.

† Before surgical removal, the surface of the lesion which was used for the second determination was washed and scrubbed repeatedly with chloroform in an attempt to remove as much extraneous fat as possible from the crypts of the lesion. This probably accounts for the lower values shown for lipids.

‡ In the report of Montgomery and Havens, the values for the various lipids, listed in the table on page 657, are expressed in milligrams per hundred grams. This obviously is in error, and we have considered these figures to represent per cent of wet tissue.

TABLE 2.—*Comparative Results of Chemical Analyses for Lipid Content of Normal Skin*

	Our Normals		Eckstein and Wile [13a]		Ramos e Silva: [5] Normal Control §	Montgomery and Havens: [4] Approximate Values for Normal Skin ‖	Ormsby and Montgomery [13b]
	First Specimen *	Second Specimen †	Cadaver White ‡	Cadaver Negro ‡			
Weight of wet tissue.....	20.50 Gm.	0.956 Gm.	....	....	0.074 Gm.		
Weight of:							
Total lipids.....	601 mg.	44 mg.					
Cholesterol.....	21 mg.	1 mg.					
Phospholipids.....	24 mg.	1.54 mg.	....	....	1.10 mg.		
Per cent of wet tissue:							
Total lipids.....	2.92	4.60	2.40	3.80	....	1 to 3	Less than 3
Cholesterol.....	0.10	0.10	0.58	0.76	....	0.10 to 0.30	
Phospholipids.....	0.12	0.16	....	....	1.50	0.10 to 0.90	
Per cent of total lipids:							
Cholesterol.....	3.50	2.28	24.10	19.90	....	Traces to 16	5 to 15
Phospholipids.....	4.00	3.50	....	....	....	10 to 30	Traces to 30

* Normal skin from abdominal wall of 22 year old white man.

† Normal skin from elbow of 21 year old white man.

‡ Normal skin from sole of cadavers.

§ Normal skin from posterior cervical region of 16 year old white girl.

‖ In the report of Montgomery and Havens, the values for the various lipids, listed in the table on page 657, are expressed in milligrams per hundred grams. This obviously is in error, and we have considered these figures to represent per cent of wet tissues.

The procedures used were Bloor's method for cholesterol levels [10] and a combination of the method of Whitehorn [11] and that of Fiske and Subbarow [12] for the phosphorus values. Table 1 shows the results of our chemical studies on cutaneous lesions of lipoidosis cutis et mucosae and a comparison with the findings reported by other investigators.[13] In table 2 we have compiled the values given for the lipid content of normal skin as presented by other authors, together with the results of our analyses.

Histology.—Material for biopsy was taken from the hyperkeratotic warty lesion on the right elbow and from the light tan plaque on the extensor surface

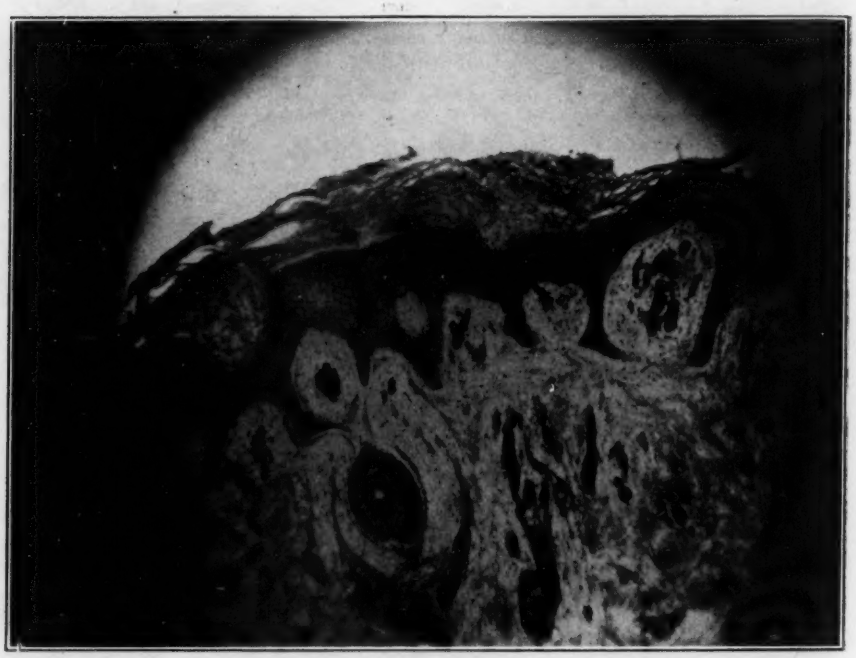

Fig. 3.—Frozen section stained with oil red O. Homogeneous deposits, rusty red color (black in photograph), are distributed diffusely throughout the corium, showing strandlike nature and dense localization about the blood vessels and appendages. × 100.

of the right forearm. Sections of the warty lesion stained with hematoxylin and eosin showed hyperkeratosis, irregular parakeratosis, irregular acanthosis and

10. Bloor, W. R.: The Determination of Cholesterol in Blood, J. Biol. Chem. **24**:227, 1916.

11. Whitehorn, J. C.: A Method for the Determination of Lipoid Phosphorus in Blood and in Plasma, J. Biol. Chem. **62**:133, 1924.

12. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

13. (*a*) Eckstein, H. C., and Wile, U. J.: The Cholesterol and Phospholipid Content of the Cutaneous Epithelium of Man, J. Biol. Chem. **44**:181, 1926. (*b*) Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1943, p. 641.

patchy spongiosis in the epidermis. The most striking and conspicuous feature was the relatively acellular, pink, opaque, homogenized material which was seen diffusely spread throughout the corium. Blood vessels were prominent, particularly in the enlarged papillae. Every vessel and appendage was surrounded by a mantle of this amorphous material. The collagen bundles were considerably diminished in amount and showed decided fragmentation.

Frozen sections prepared with oil red O stain for fat (fig. 3) showed that the amorphous material which was seen in the hematoxylin and eosin-stained sections took a rusty red color, contrasting with the brilliant orange-red of the fat in the follicles. This rusty red-stained material appeared densest about the blood vessels but also was seen diffusely distributed throughout the corium and as light streaks intimately combined with the loose, acellular, connective tissue. Conspicuous was the absence of any appreciable cellular infiltrate or inflammatory reaction. No foam cells or necrosis was present.

The sections made from the biopsy specimen taken from the plaque on the right forearm showed essentially the same changes in the corium. However, there was little modification of the epidermis, and the papillae were not enlarged.

COMMENT

The history and findings in this case were similar in many respects to those which have been previously reported. The cardinal features of early hoarseness, lesions of the mucous membrane, characteristic involvement of the tongue, dental anomalies and nodular and verrucous cutaneous manifestations were present. The microscopic sections showed homogeneous material distributed throughout the corium and its distinctive localization about blood vessels. Oil red O stain for fat gave this material a rusty red color, which was in contrast with the brighter orange-red of the lipid substances ordinarily seen in the hair follicles and subcutaneous fat tissues.

In this disease, infiltrations in the mucous membranes may involve certain structures, so that obstructive phenomena ensue. That complications of a serious nature arise is indicated by the necessity for laryngotomy to prevent asphyxia in 8 of the 14 cases compiled by Urbach. In his report, Sulzberger [14] described recurrent painful swellings of the parotid gland. He stated, "It is apparent that the swellings are due to valve-like occlusion of the parotid duct, probably by the masses of lipoid protein' in this area of the mucous membrane." The orifice of Stenson's duct was reported as elevated and reddened. Our patient recounted similar episodes of swellings of the parotid gland, and examination of the mouth revealed enlarged papillae of the parotid ducts. Mention has been made of the hypertrophied lacrimal papillae exhibited by our patient. Although no blockage to tear drainage occurred here, it can be assumed that in the mouth infiltrations about the orifice of the parotid duct may be responsible for obstructive phenomena. Undoubtedly other

14. Sulzberger, M. B.: A Case of Lipoidosis Cutis et Mucosae: So-Called "Lipoid Proteinosis," Urbach-Wiethe, Laryngoscope **52**:286, 1942.

factors, such as infection or trauma, contribute to the occlusion by the addition of edema to a nonelastic tissue.

Other observers have suggested that lipoidosis cutis et mucosae is a systemic disease, but thus far the only suggestive evidence for this concept is Bazex's [15] demonstration in an excised ectopic testicle of sudanophilic material surrounding the blood vessels. Concomitant diabetes mellitus has been found in some of the patients with this disease, but this is by no means a constant finding. Urbach postulated that infiltrations in the pancreas could account for the disturbed carbohydrate metabolism. Wile and Snow demonstrated considerable retention of sulfabromophthalein as evidence of impaired hepatic function in their case. Although we are hesitant to accept the small values for sulfobromophthalein retention which we uncovered in our studies as evidence of hepatic disease, inasmuch as none of the other tests for hepatic function gave abnormal results, some significance should be attached to this finding. Certainly consideration must be given to the possibility that the same kind of infiltration that affects the skin, mucous membranes and testes may also involve the liver. This aspect of the disease should be investigated by future observers.

There has been frequent reference made in many of the reports to "eczema," "sores," "pustules," "crust-covered ulcers," "sore mouth" and "painful ulcers on the tongue," which, according to the histories, appeared early during the course of the disease. These primary lesions have also beeen observed occurring later in life, and it was the opinion of Ramos e Silva that the scars on the skin in fully developed conditions resulted from the primary ulcerations. We are in accord with this belief, for it was possible to follow the course of the crusted ulcers, which our patient presented on admission, to the depressed scars which finally evolved. The preceding bullous eruption had been considered as erythema multiforme bullosum in the overseas hospital from which he had been transferred. While the patient was under our observation, a pea-sized superficial bleb developed under the edge of a plaster of paris cast which had been applied to the arm after excision of the lesion on the elbow. This lesion promptly healed under sterile dressings and left no scar. Subsequent attempts to reproduce blebs on the skin by rubbing were unsuccessful, and patch tests with sulfur ointment elicited negative reactions.

Now, we may refer to the chemical nature of these deposits in the corium, which are the essential features of the histologic picture. In our chemical determinations, no increase in the phosphatide fraction was revealed such as was found by Montgomery and Havens and Ramos e Silva. Our results were more like those of Wile and Snow and Hansen.

15. Bazex, A.: Un cas de lipoïdo-protéinose (maladie de Urbach-Wiethe), Bull. Soc. franç. de dermat. et syph. **46**:136, 1939.

In fact, the total percentage of lipids and phospholipids in wet tissue was lower in the diseased skin than in that of normal controls. There was a slight increase in the actual cholesterol content of the lesions and a greater increase in the cholesterol percentage of the total lipid as compared with that in our controls. Reference to table 1 will show the wide discrepancies in the results of the various analyses. From table 2, it can readily be seen that the values given for normal skin present wide ranges. The standards accepted by Ramos e Silva and Montgomery and Havens for the phospholipid per cent of normal skin are much higher than those which we found. Different methods of analysis may account for these discrepancies and make for difficulty in comparing results. In evaluation of chemical analyses for lipids in the skin, the age of the person from whom the specimen is obtained, the site of the skin and the type of cutaneous lesion must be considered. We should like to point out one particular possibility for error, which was developed during our chemical studies. The lesion on the elbow which was used for the first determination was prepared preoperatively in the usual manner before excision. However, before the lesion on the other elbow was removed, it was washed thoroughly with soap and water and then scrubbed repeatedly with chloroform in an attempt to remove as much fat as possible from the verrucous crypts. Final chloroform washings still gave reactions for cholesterol. This special treatment reflected itself in a considerable reduction in the amount of lipid material later extracted. It is concluded, therefore, that chemical determinations on verrucous types of lesions do not give an accurate appraisal of the actual lipid content of the tissues.

SUMMARY AND CONCLUSION

Another case of lipoidosis cutis et mucosae (lipoid proteinosis [Urbach-Wiethe]) is reported. The cardinal features of early hoarseness, lesions of the mucous membrane, characteristic involvement of the tongue and frenum, dental anomalies and nodular and verrucous cutaneous manifestations are described. The histologic changes are in accord with those of other authors, but the results of chemical analyses do not substantiate the concept that the disease is due to deposits of lipids. There was no increase in the lipoidal components of the diseased tissue. Attention is directed to the pitfalls in evaluation of chemical analyses done on verrucous tissue.

The complications of obstruction due to deposits about ducts and in papillae, such as involves Stenson's duct, is commented on.

The retention of sulfobromophthalein suggests the possibility of hepatic involvement and fits in with the concept that the disease is of a generalized nature.

TOPICAL TREATMENT WITH PENICILLIN OINTMENT

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THE PARENTERAL use of penicillin has now reached the stage at which its efficacy in a wide variety of diseases has been well established, although its full clinical possibilities as a local therapeutic agent are yet to be realized.

Franks, Dobes and Romano [1] have reported dramatic results in the treatment of 8 patients with impetigo contagiosa. Others who have reported good results in the treatment of impetigo are Kierland,[2] Garrod,[3] Roxburgh, Christie and Roxburgh [4] and Templeton, Clifton and Seeberg.[5] Florey and Florey [6] found penicillin ointment of value in the treatment of mixed infections of chronic wound sinuses. Johnson [7] has reported excellent results in the treatment of 25 patients with common pyodermas. Roxburgh, Christie and Roxburgh [4] used a penicillin ointment to treat 15 patients with sycosis barbae, obtaining permanent cures in 5 and initial cures in 3, with relapse and permanent cure following a second course of penicillin ointment. Treatment of the other 7 patients was either a failure or caused irritation of the skin. May [8] treated 50 patients with staphylococcic infections of the skin, including many with sycosis barbae, and obtained effective results. Cooke [9] reported 14 cases of uncomplicated sycosis vulgaris successfully cleared with a spray of crude penicillin filtrate.

From the Department of Dermatology, Temple University School of Medicine.

1. Franks, A. G.; Dobes, W. L., and Romano, D.: Penicillin in the Treatment of Cutaneous Disease, Arch. Dermat. & Syph. **52**:14 (July) 1945.

2. Kierland, R. R.: Local Use of Penicillin Preparations: Cutaneous Diseases, Mil. Surgeon **97**:57 (July) 1945.

3. Garrod, L. P.: Penicillin, St. Barth. Hosp. J. **48**:113 (Aug.) 1944.

4. Roxburgh, I. A.; Christie, R. V., and Roxburgh, A. C.: Penicillin in Treatment of Certain Diseases of the Skin, Brit. M. J. **1**:524 (April 15) 1944.

5. Templeton, H. J.; Clifton, C. E., and Seeberg, V. P.: Local Application of Penicillin for Pyogenic Dermatoses, Arch. Dermat. & Syph. **51**:205 (March) 1945.

6. Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1**:387 (March 27) 1943.

7. Johnson, H. M.: Penicillin Therapy of Impetigo Contagiosa and Allied Diseases, Arch. Dermat. & Syph. **50**:1 (July) 1944.

8. May, H. B.: Penicillin in Civilian Practice, Brit. M. J. **2**:817 (Dec. 23) 1944.

9. Cooke, M. A.: Penicillin in Sycosis Barbae, Lancet **1**:543 (April 28) 1945.

Our objective in this study was to ascertain the results obtained in the treatment of a variety of superficial dermatoses with penicillin locally in the form of an ointment consisting of 1,000 Oxford units of calcium penicillin per gram in a base of hydrous wool fat and white petrolatum.[10]

Patients were instructed to apply the ointment liberally three to four times daily on the infected areas, and in other instances dressings were employed, which were changed twice daily. All patients were advised to keep the ointment continually refrigerated.

In the following report of the results of local penicillin therapy, the organisms present were not tested for sensitivity to penicillin. We are well aware of the indications for the use of penicillin. Selecting

Impetigo contagiosa. *A*, appearance on Sept. 10, 1945, before application of penicillin ointment; *B*, appearance on September 12, forty-eight hours after the beginning of treatment.

these cases at random does not imply that we have employed the penicillin ointment indiscriminately, nor do we wish to discredit its use, being cognizant of the fact that negative results were expected in many instances. However, these negative results are significant in bearing out the consensus among American clinicians who favor the administration of penicillin by the parenteral route rather than by topical application for all but the most superficial lesions.

Our group of 131 patients had miscellaneous infections, including impetigo, intertrigo (mixed infections), eczematoid dermatitis, paro-

10. The preparation used was Topicillin, supplied by E. R. Squibb & Sons.

nychia, sycosis vulgaris, ulcer, carbuncle, furuncle, ecthyma, molluscum contagiosum, rosacea, dermatophytosis and seborrheic dermatitis.

The accompanying table is presented to show the results obtained by the topical application of a penicillin ointment in this group of 131 patients with various infections of the skin. It will be quickly noted that what might be considered satisfactory results were obtained only against impetigo contagiosa and ecthyma and 50 per cent good results against superficial folliculitis. Impetigo may clear up in as short a time as one to three days, and it is our opinion that penicillin may be considered ineffective if there is not a decided improvement by the end of the third day. In ecthyma improvement may not be definite until the end of a week of therapy.

Analysis of Results for Patients Treated with Penicillin Ointment

Diagnosis	No. of Patients	Cured	Made Worse	Unimproved	Improved
Impetigo contagiosa	25	21	2	2	..
Intertrigo (ears)	23	2	8	13	..
Infectious eczematoid dermatitis	7	..	..	5	2
Paronychia	5	..	..	4	1
Acne vulgaris	5	..	..	5	..
Moniliasis	10	..	5	5	..
Superficial folliculitis	12	6	2	4	..
Sycosis vulgaris	8	..	2	6	..
Ulcers	13	..	..	13	..
Furunculosis	6	..	..	5	1
Carbunculosis	2	..	..	2	..
Ecthyma	8	8	..	..	..
Molluscum contagiosum	2	..	..	2	..
Rosacea	1	..	..	1	..
Dermatophytosis	2	..	..	2	..
Seborrheic dermatitis	2	..	..	2	..

REACTIONS

Pyle and Rattner [11] reported a case of contact dermatitis in an army medical officer who was preparing solutions of penicillin and administering the drug to patients. The eyelids, face, fingers and penis were affected. The dermatitis subsided when contact with the penicillin was eliminated. The patch test elicited a positive reaction. When he was again exposed to the penicillin, the dermatitis recurred.

Binkley and Brockmole [12] reported cases of 2 hospital interns in whom contact dermatitis on the face and hands developed. The eruption disappeared when exposure to a solution of penicillin was avoided.

11. Pyle, H. D., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125**:903 (July 29) 1944.

12. Binkley, G. W., and Brockmole, A.: Dermatitis from Penicillin, Arch. Dermat. & Syph. **50**:325 (Nov.) 1944.

Silvers [13] reported the case of a chemist sensitive to penicillin. A contact dermatitis on the eyelids and penis developed. The patch test with yellow amorphous sodium penicillin elicited a positive reaction. A patch test with the solution of pure white crystalline sodium penicillin elicited a negative reaction. The author concluded that the impurities present in the yellow amorphous sodium penicillin were responsible for the contact dermatitis.

In many of our patients penicillin ointment appeared to irritate the skin. We attempted to ascertain which constituent of the ointment was responsible by applying to our so-called sensitive patients patch tests with the penicillin ointment per se, hydrous wool fat and petrolatum. We were unable to elicit any positive reactions to the patch tests.

In 1 patient whom we treated for sycosis vulgaris, the local application of penicillin ointment produced not only an exacerbation of the existing eruption but a decided erythematous reaction. In this patient we were unable to elicit positive reactions to patch tests with the penicillin ointment and with the controls employed. After the subsidence of the dermatitis following the avoidance of the penicillin ointment, we were interested in determining whether the patient had been made sensitive to penicillin. To determine this, we had him use the penicillin ointment again, with a similar disastrous experience. After permitting the superimposed dermatitis to heal, we gave him 25,000 units of penicillin parenterally, which did not produce any exacerbation of the preexisting condition or influence it in any other manner.

We are at a loss to explain the irritation produced by the penicillin ointment.

COMMENT

Our results for 131 patients treated with penicillin ointment may be classified as follows:

Twenty-one of a total of 25 patients suffering with impetigo contagiosa were entirely cured within three days. Only 2 of 23 patients with intertriginous dermatitis of the ears (mixed infections) responded favorably to topically applied penicillin ointment. None of the 7 patients with infectious eczematoid dermatitis were cured. In 5 patients with acne vulgaris the treatments were complete failures. Ten patients with moniliasis did not respond to the treatment.

Six of 12 patients with superficial folliculitis (simple) responded to treatment. For 8 patients with sycosis vulgaris treatment resulted in utter failure. No improvement was noted in 13 patients exhibiting varicose, phagedenic, superficial pyogenic ulcers and ulcers secondary to roentgen dermatitis.

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13. Silvers, S. H.: Contact Dermatitis from Amorphous Sodium Penicillin, Arch. Dermat. & Syph. **50**:328 (Nov.) 1944.

There was an improvement in the condition of 6 patients suffering with furunculosis and 2 patients suffering with carbunculosis, but no cures were effected in this group.

Eight patients with ecthyma responded dramatically to treatment. The treatment of 2 patients with molluscum contagiosum gave negative results. Negative response to treatment was observed in 1 patient with rosacea, 2 patients with dermatophytosis and 2 patients with extensive seborrheic dermatitis.

Penicillin ointment is of value chiefly in the treatment of impetigo contagiosa and ecthyma.

AGRANULOCYTOSIS

Report of Twelve Cases in Which It Followed Intensive Arsenotherapy for Syphilis

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AGRANULOCYTOSIS, in our experience, has been a rather frequent and annoying complication during the course of treatment of syphilis by intensive methods. This paper concerns itself with a report of 12 cases in which this complication was encountered, covering a period of one year.[1] It occurred in the course of therapy based on the following regimens:

1. Oxophenarsine hydrochloride and bismuth subsalicylate—multiple injections on a twenty-five day schedule: Oxophenarsine hydrochloride (mapharsen) was administered six days a week for a total of twenty-two injections, with a maximum individual dose of 60 mg., and bismuth subsalicylate in oil was administered concurrently, 200 mg. every five days.
2. Oxophenarsine hydrochloride and bismuth subsalicylate—multiple injections on a twenty day schedule (Schock method): One dose of oxophenarsine hydrochloride was given daily for twenty consecutive days, the maximum dose being 70 mg., and bismuth subsalicylate in oil was administered concurrently 200 mg. every five days.
3. Penicillin, oxophenarsine hydrochloride and bismuth subsalicylate—multiple injections on an eight day schedule: Ten thousand units of penicillin was injected every three hours for

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Dr. Fisher was formerly Surgeon, Dr. Holley, Passed Assistant Surgeon, and Dr. Fein, Passed Assistant Surgeon in the United States Public Health Service.

Under the supervision of Senior Assistant Surgeon Evert A. Swensson, Medical Officer in Charge from November 1943 to August 1944, many of the patients with agranulocytosis were treated. Dr. Swensson is now serving in the Pacific area with the United States Public Health Service.

1. The work reported on was done while the authors were connected with the United States Public Health Service at Durham, N. C. The patients concerned were treated at the United States Public Health Service Medical Center in Durham, N. C.

a total dose of 600,000 units; one dose of oxophenarsine hydrochloride, every day for eight days, with a maximum dose of 60 mg., and one dose of bismuth subsalicylate in oil, 200 mg., on the first, fifth and eighth days.

One thousand, eight hundred and eighty-two syphilitic patients were treated according to the aforementioned schedules. Of this number, 504 were treated according to the twenty-five day schedule, 483 according to the twenty day schedule and 895 according to the eight day schedule (penicillin–oxophenarsine hydrochloride–bismuth). The locytosis developed in 11 patients; 8 were on the twenty-five day schedule, 2 were on the twenty day schedule and 1 was on the eight day schedule (penicillin–oxophenarsine hydrochloride–bismuth). The twelfth patient (case 9 under the "Report of Cases" in this paper and patient 9 in the table) entered the hospital because of a complication occurring in the course of weekly injections of neoarsphenamine and was found to have agranulocytosis. It must also be noted that a total of 58 other patients did not complete treatment because of some intolerance of oxophenarsine hydrochloride: 16 on the twenty-five day schedule, 28 on the twenty day schedule and 14 on the eight day (penicillin-oxophenarsine hydrochloride-bismuth) schedule. With most of these treatment was discontinued because of a febrile reaction, and it might be assumed that some would have been candidates for agranulocytosis had treatment not been interrupted.

SYMPTOMS

The histories of these patients were not unusual. There was no mention of sensitivity to any drug, although 50 per cent of the patients had been previously treated with arsenicals. The type of onset in most of the cases was classic, with general malaise, headache, fever and a sore throat. However, in 2 cases there was no pharyngitis—neither concomitant with nor after the febrile reaction. In 6 cases there was a previous febrile reaction which might have served as a warning. In 2 of these cases the complication was preceded by symptoms of erythema of the ninth day—fever, general malaise, conjunctivitis and a scarlatiniform eruption—and in 4 cases there was a febrile reaction not associated with any complaints or change in the blood count. The arsenotherapy was discontinued for from one to five days and then resumed, and after that the rise of temperature was again manifest, and agranulocytosis ensued. In 3 cases the agranulocytosis was ushered in by the rise of temperature without previous premonitory signs. In 3 cases agranulocytosis was incidentally discovered during a routine blood count.

In the 10 cases in which treatment was based on the twenty and twenty-five day methods, agranulocytosis occurred in the last half or near the end of the scheduled course of treatment.

The acompanying table gives pertinent information as to the diagnosis, the previous treatment, the treatment for syphilis given at this institution and the number of doses of the arsenical administered before agranulocytosis ensued.

Data on the Patients Treated and on the Therapy Preceding the Reactions

Patient	Race	Sex	Age, Yr.	Diagnosis of Syphilis	Previous Treatment *	Treatment Schedule	No. of Doses Preceding Reaction
1	N	M	39	Primary seropositive	4 arsenical (type ?)	20 day 20 Gm. of sulfathiazole	18
2	N	F	18	Early latent	None	25 day	20
3	N	F	19	Secondary	1 oxophenarsine hydrochloride	20 day	15
4	N	F	17	Early latent	1 oxophenarsine hydrochloride, 165 mg. bismuth subsalicylate	25 day	13
5	N	F	15	Early latent	None	25 day	15
6	N	F	18	Secondary	None	25 day	19
7	N	F	18	Secondary with pregnancy	None	25 day	19
8	N	M	19	Secondary	0.3 Gm. neoarsphenamine, 200 mg. bismuth subsalicylate, 20 Gm. sulfathiazole for gonococcic infection	Pen-ox-bis †	8
9	N	F	19	Secondary	4 arsenical, 4 bismuth subsalicylate	Admitted with agranulocytosis after 4 weekly injections of neoarsphenamine	
10	N	F	25	Early latent	None	25 day	20
11	N	F	17	Early latent, with pregnancy	None	25 day	20
12	N	F	20	Early latent	1 oxophenarsine, hydrochloride	25 day sulfathiazole for gonococcic infection	18

* The numbers represent injections.
† Pen-ox-bis is an abbreviated form for penicillin-oxphenarsine hydrochloride-bismuth schedule.

LABORATORY FINDINGS

A routine blood count and a urinalysis were made when the patient was admitted to the hospital and every five days thereafter. All the patients had normal blood counts on admission with the exception of the one in case 9, who was admitted with agranulocytosis. The patient in case 1 had no blood count on admission. In all the cases in which the reaction developed, the blood count showed leukopenia, with complete absence or decided reduction of granulocytes.

COURSE AND TREATMENT

The course of illness was variable. In cases 1, 3 and 4 toxicity was high and the course stormy, and in the others there were milder symptoms of toxicity. The fever lasted from five to fourteen days. The blood counts returned to normal soon after the febrile reaction had been dissipated.

Treatment consisted in all cases of the administration of pentnucleotide (10 cc. every six hours, intramuscularly injected), liver extract [2] (2 cc. daily, intramuscularly, injected) and dimercaprol ("BAL;" 2,3-dimercaptopropanol) [3] (1.5 cc. every six hours for forty-eight hours and then 2 cc. daily for six doses, intramuscularly injected). In 3 cases multiple transfusions were administered in addition. General supportive measures included intravenous administration of a 5 per cent solution of dextrose to maintain the water balance, mouth washes of sodium perborate to decrease secondary infection, and vitamin therapy.

COMMENT

Blood dyscrasias occurring during the course of therapy with trivalent arsenicals are considered rare,[4] but might be found more frequently if periodic examinations were made of the blood of patients under treatment. It has also been reported that aplastic anemia and agranulocytosis are extremely rare in Negroes.[5] The patients whose agranulocytosis is reported in this paper have all been of the Negro race. (Seventy-five per cent of the patients treated at this center are Negroes.) The mortality rate in cases of agranulocytosis has been estimated at 48 per cent by one author [6] and as high as 70 per cent by another.[7] In this group of patients there were no deaths, and all made an uneventful recovery.

SUMMARY

Eleven cases in which agranulocytosis occurred during intensive arsenotherapy for syphilis are reported. One case is reported in which this complication occurred in the course of routine orthodox weekly injections of neoarsphenamine. Fifty per cent of the patients had received no previous therapy for syphilis. The reaction occurred in all cases toward the end of the scheduled course of treatment. Immediate cessation of the administration of arsenicals followed, and therapy with dimercaprol, pentnucleotide and liver extract and, in the more severe

2. Axelrod, A. E.; Gross, P.; Bosse, M. D., and Swingle, K. F.: Treatment of Leucopenia and Granulopenia in Rats Receiving Sulfaguanidine in Purified Diets, J. Biol. Chem. **148**:721, 1943.

3. An experimental arsenodiuretic supplied by Surgeon Harry Eagle, United States Public Health Service, through the Office of Scientific Research and Development.

4. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1942, p. 478.

5. Irgang, S.: Gastric Intolerance Accompanying Arsphenamine Therapy, Am. J. Syph., Gonor. & Ven. Dis. **25**:241, 1939.

6. Loveman, A. B.: Toxic Granulocytopenia, Purpura Hemorrhagica, and Aplastic Anemia Following Arsphenamines, Ann. Int. Med. **5**:1238, 1932.

7. Reznikoff, P.: Agranulocytosis and Leukopenia, J. A. M. A. **115**:128 (July 13) 1940.

cases, blood transfusions were instituted. There were no deaths. The cases reported emphasize the importance of a close survey of all patients receiving arsenicals, with particular observation of the temperature and with routine blood counts. In 50 per cent of the cases the agranulocytosis occurred after there had been a febrile reaction of the "erythema of the ninth day type" or fever alone.

REPORT OF CASES

CASE 1.—O. F., a Negro man aged 39, was admitted to the hospital on Feb. 22, 1944, with a diagnosis of primary syphilis, seropositive, previously treated. He was treated according to the twenty day schedule, receiving 70 mg. of oxophenarsine hydrochloride daily. On the patient's admission a blood count was not made. The urine was essentially normal.

The patient tolerated oxophenarsine hydrochloride well, with the exception of mild headache and nausea following each injection. In addition to this drug, he also received 4 Gm. of sulfathiazole a day for five days because of the secondary infection in the primary lesion. After the eighteenth injection of oxophenarsine hydrochloride he had a temperature of 102.4 F. and complained of a sore throat. Examination revealed a necrotic lesion on each tonsil. The white blood cell count was 2,600, and there was a complete absence of granulocytes. He was given a blood transfusion (500 cc.) and dimercaprol. The next day the white blood cell count was 1,000, and there was still a complete absence of granulocytes. He was given a second transfusion, liver extract intramuscularly, sulfathiazole chewing gum, ascorbic acid, pentnucleotide, nicotinic acid and other supportive measures. He continued to have a septic temperature, reaching 105 F., for six days, after which the temperature returned to normal. The white blood cells increased in number, and granulocytes reappeared in the circulating blood. On the seventh day following the reaction, the white blood cell count was 6,320, and there were 58 per cent polymorphonuclear neutrophils, 38 per cent lymphocytes and 4 per cent monocytes. The patient made an uneventful recovery.

CASE 2.—E. G., a Negro woman aged 18, was admitted to the hospital on July 15, 1944, with a diagnosis of early latent syphilis, not previously treated. She was treated according to the twenty-five day schedule, receiving 55 mg. of oxophenarsine hydrochloride daily. On her admission the hemoglobin content was 75 per cent; the white blood cell count was 6,300, and there were 60 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 36 per cent lymphocytes and 2 per cent monocytes. The urine was essentially normal.

The patient tolerated oxophenarsine hydrochloride well until the eighth dose, at which time her temperature rose to 102 F. The blood count and the urinalysis showed no abnormalities. Treatment was withheld for one day, and small trial doses of the drug were given on the following three days without any rise in temperature; hence, the full schedule was resumed. Following the twentieth dose of the drug, a routine blood count showed the white blood cell count to have fallen to 3,000, with a complete absence of granulocytes, 73 per cent lymphocytes and 27 per cent monocytes. At this time her temperature was elevated to 100.2 F. However, she had no complaints. Treatment with oxophenarsine hydrochloride was discontinued. On the following day her temperature rose to 103.6 F., and there was still an absence of granulocytes. She was given liver intramuscularly, pentnucleotide and dimercaprol. Her temperature remained elevated for three days and then returned to 99 F. Granulocytes reappeared in the circulating blood

at the same time, so that within four days the hemoglobin content was 73 per cent and the white blood cell count 6,400, with 44 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 44 per cent lymphocytes and 10 per cent monocytes. Her recovery was uneventful.

CASE 3.—L. C., a Negro woman aged 19, was admitted to the hospital on Feb. 26, 1944, with a diagnosis of secondary syphilis, previously treated. She was given treatment according to the twenty day schedule, receiving 50 mg. of oxophenarsine hydrochloride daily.

The patient tolerated the drug well until the tenth dose, at which time she complained of nausea and vomiting. At that time it was noted that her temperature was elevated to 100 F. and that there was some injection of the conjunctivas. Treatment was withheld for one day, after which a small trial dose of the drug was administered. This was apparently well tolerated, and treatment was resumed. After the fifteenth dose of the drug, the patient suffered a severe chill, and her temperature rose to 105 F. The administration of oxophenarsine hydrochloride was discontinued. Physical examination revealed decided pharyngitis. On the morning of the same day the hemoglobin content was 85 per cent, and the white blood cell count was 6,100, with 65 per cent polymorphonuclear neutrophils and 35 per cent lymphocytes. That night at 10:30 a blood count revealed 2,000 white blood cells per cubic millimeter; 10 per cent were polymorphonuclear neutrophils, 50 per cent lymphocytes and 40 per cent monocytes. On the following day the red blood cell count was 4,200,000 and the white blood cell count 2,450, with no polymorphonuclear neutrophils, 2 per cent basophils, 4 per cent eosinophils, 47 per cent lymphocytes and 47 per cent monocytes. On the third day following the reaction the red blood cell count was 3,820,000 and the white blood cell count 2,020, with a complete absence of granulocytes, 55 per cent lymphocytes and 45 per cent monocytes. The patient experienced a stormy course with a septic temperature and necrotic pharyngitis for fourteen days. She was given liver intramuscularly, pentnucleotide, dimercaprol, vitamin C and penicillin, as well as general supportive measures. On the eleventh day following the reaction, the hemoglobin content was 82 per cent, and the white cell count was 5,600, with 21 per cent polymorphonuclear neutrophils, 75 per cent lymphocytes and 4 per cent monocytes. The blood count returned to normal on the fourteenth day. The patient made an uneventful recovery.

CASE 4.—H. P., a Negro girl aged 17, was admitted to the hospital on Oct. 9, 1944, with a diagnosis of early latent syphilis, previously treated. She was given the twenty-five day treatment, receiving 50 mg. of oxophenarsine hydrochloride daily. On the patient's admission, the hemoglobin content was 90 per cent and the white blood cell count was 6,300, with 60 per cent polymorphonuclear neutrophils, 38 per cent lymphocytes and 2 per cent monocytes. The urine was essentially normal.

The patient tolerated the drug well until the ninth dose, at which time she complained of itching of the feet and the back but no eruption could be seen. Her temperature was elevated to 100.6 F. At this time, the hemoglobin content was 88 per cent, and the white blood cell count was 4,600, with 38 per cent polymorphonuclear neutrophils, 58 per cent lymphocytes and 4 per cent monocytes. The drug was withheld for one day, after which the patient received a small trial dose, from which there was no apparent reaction. Treatment was then resumed with the full dose of oxophenarsine hydrochloride without difficulty until she had received the thirteenth injection. Her temperature then rose suddenly to 104.6 F., and she complained of general malaise and sore throat. The hemo-

globin content was 87 per cent, and the white blood cell count was 3,600, with 6 per cent polymorphonuclear neutrophils, 82 per cent lymphocytes and 12 per cent monocytes. There was moderate pharyngitis, with a grayish exudate covering both tonsils. The administration of the drug was immediately discontinued, and the patient was given liver intramuscularly, pentnucleotide and dimercaprol. Her temperature remained elevated for three days, after which it returned to normal, and by the fourteenth day the hemoglobin content was 88 per cent, while the white blood cell count was 5,000, with 46 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 39 per cent lymphocytes and 14 per cent monocytes. The patient made an uneventful recovery.

CASE 5.—G. R., a Negro girl aged 15, was admitted to the hospital on July 17, 1944, with a diagnosis of early latent syphilis, not previously treated. She was treated according to the twenty-five day schedule, receiving 50 mg. of oxophenarsine hydrochloride daily. On admission, the red blood cell count was 3,600,000, and the white blood cell count was 10,000, with 69 per cent polymorphonuclear neutrophils and 31 per cent lymphocytes. The urine was essentially normal.

The patient tolerated the drug well until the seventh dose, when she complained of headache, and her temperature was elevated to 100 F. The patient remained under treatment in spite of this elevation, which continued until the eleventh dose. At this time there appeared on the extensor surfaces of the forearms and the thighs a fine papular nonpruritic eruption. The patient's temperature was again 100 F. This was interpreted as erythema of the ninth day. Oxophenarsine hydrochloride was withheld for two days, after which treatment was resumed. After the fifteenth dose there was a brisk rise of temperature, reaching 102.2 F., and the patient complained of a sore throat. On the following day a necrotic exudate was observed in the pharynx. On this day the red blood cell count was 3,850,000 and the white blood cell count 3,800, with no polymorphonuclear neutrophils, 2 per cent eosinophils, 78 per cent lymphocytes and 20 per cent monocytes. Treatment consisted of the administration of liver extract by intramuscular injection and of pentnucleotide and dimercaprol, as well as supportive measures. The patient's temperature remained septic for the next three days and returned to normal by lysis on the fifth day. On that day granulocytes reappeared in the blood; there were 7,400 white blood cells, with 54 per cent polymorphonuclear neutrophils, 10 per cent eosinophils, 30 per cent lymphocytes and 6 per cent monocytes. The patient made an uneventful recovery.

CASE 6.—H. C., a Negro woman aged 18, was admitted to the hospital on April 24, 1944 with a diagnosis of secondary syphilis, not previously treated. She was treated according to the twenty-five day schedule, receiving a daily dose of 55 mg. of oxophenarsine hydrochloride. On her admission the hemoglobin content was 82 per cent and the white blood cell count 6,400. A differential count was not made. The urine was normal. Following the nineteenth injection of the drug the patient complained of chilly sensations and dysphagia. Her temperature was elevated to 102.4 F.; the pharynx was edematous, and there was a necrotic membrane over each tonsil. The cervical lymph nodes were enlarged and tender. The hemoglobin content was 75 per cent, the red blood cell count was 4,300,000, and the white blood cell count was 4,100, with a complete absence of granulocytes, 60 per cent lymphocytes and 40 per cent monocytes. A smear taken from the pharynx showed a few fusiform bacilli, a moderate number of large spirochetes and a few pus cells. The injections of oxophenarsine hydrochloride were discontinued, and the patient was given pentnucleotide, liver extract intramuscularly and dimercaprol. In addition she was given two blood transfusions. On the fifth day, her temperature fell by

lysis, and the peripheral blood showed a few granulocytes for the first time. On the ninth day the patient was afebrile, and the white blood cell count was 7,700, with 38 per cent polymorphonuclear neutrophils, 10 per cent eosinophils, 40 per cent lymphocytes and 12 per cent monocytes. The patient made an uneventful recovery.

Case 7.—E. W., a Negro woman aged 18, was admitted to the hospital on Sept. 9, 1944, with a diagnosis of secondary syphilis, not previously treated, and pregnancy. She was treated according to the twenty-five day schedule, receiving 55 mg. of oxophenarsine hydrochloride daily. On her admission the hemoglobin content was 78 per cent and the white blood cell count 8,500, with 63 per cent polymorphonuclear neutrophils and 37 per cent lymphocytes. The urine was essentially normal.

The patient tolerated the drug well, with the exception that her temperature rose daily to between 99 and 100 F. Following the nineteenth injection of the drug, there was a brisk rise in temperature, reaching 102.4 F. The patient complained of a sore throat. On examination she was found to have a necrotic membrane on each tonsil and large tender cervical lymph nodes. At this time, the hemoglobin content was 77 per cent, and the white blood cell count was 3,100, with 7 per cent polymorphonuclear neutrophils, 68 per cent lymphocytes and 25 per cent monocytes. The administration of oxophenarsine hydrochloride was discontinued, and the patient was given pentnucleotide, liver intramuscularly and dimercaprol. On the following day the white blood cell count was 3,700, with 5 per cent polymorphonuclear neutrophils, 65 per cent lymphocytes and 30 per cent monocytes. The patient's temperature remained elevated for five days and returned to normal by lysis. At the same time the granulocytes increased rapidly, so that by the fifth day following the reaction the white blood cell count was 8,500, with 50 per cent polymorphonuclear neutrophils, 40 per cent lymphocytes and 10 per cent monocytes. The patient made an uneventful recovery.

Case 8.—J. D., a Negro youth aged 19, was admitted to the hospital with a diagnosis of secondary syphilis, previously treated, and acute gonorrheal urethritis. The previous treatment consisted of 0.3 Gm. of neoarsphenamine, 200 mg. of bismuth and 20 Gm. of sulfathiazole. He was treated according to the penicillin-oxophenarsine hydrochloride-bismuth schedule, receiving 60 mg. of oxophenarsine hydrochloride daily. On the patient's admission the hemoglobin content was 95 per cent and the white blood cell count 6,000, with 52 per cent polymorphonuclear neutrophils and 48 per cent lymphocytes. The urine was essentially normal.

The patient tolerated oxophenarsine hydrochloride well until the sixth dose, at which time his temperature was elevated to 102.6 F. The white blood cell count at this time was 7,000, with 75 per cent polymorphonuclear neutrophils and 25 per cent lymphocytes. Although the drug was omitted, the patient's temperature continued to rise, reaching a peak of 105 F. within forty-eight hours; it then fell by lysis, reaching normal on the sixth day after the onset of the reaction. On the tenth day following the discontinuance of arsenotherapy, the patient was again given 60 mg. of oxophenarsine hydrochloride. On the next day the last and eighth dose was given. His temperature immediately rose to 101 F., and the white blood cell count was 3,800, with 5 per cent polymorphonuclear neutrophils, 11 per cent eosinophils, 74 per cent lymphocytes and 10 per cent monocytes. The patient was given liver extract intramuscularly, pentnucleotide and dimercaprol. Four days later the white blood cell count was 4,800, with 4 per cent polymorphonuclear neutrophils, 9 per cent eosinophils, 63 per cent lymphocytes and 24 per

cent monocytes. Daily blood counts showed a progressive rise in the number of leukocytes as well as in the percentage of granulocytes.

During this whole episode the patient was never extremely uncomfortable, nor did he ever have pharyngitis. The white blood cell count when he was discharged from the hospital, two weeks after the onset of symptoms, was 8,000, with 64 per cent polymorphonuclear neutrophils and 36 per cent lymphocytes. He made an uneventful recovery.

CASE 9.—J. B. G., a Negro woman aged 19, was admitted to the hospital on June 12, 1944 with a diagnosis of a febrile reaction following the fourth injection of neoarsphenamine for the treatment of secondary syphilis while under the care of a private physician. On admission, she appeared toxic, her temperature was 104 F., and she had necrotic ulcerative lesions of the pharynx and the tonsils. The hemoglobin content was 55 per cent; the red blood cell count was 3,200,000, and the white blood cell count was 4,800, with 14 per cent polymorphonuclear neutrophils, 5 per cent eosinophils, 61 per cent lymphocytes and 20 per cent monocytes. These findings suggested the diagnosis of agranulocytosis. A blood count on the following day was essentially the same. The patient was given pentnucleotide, dimercaprol and nicotinic acid, with other supportive measures. Her temperature remained elevated for one week and fell by lysis. During this period the number of granulocytes increased so that one week after the patient's admission to the hospital, the white blood cell count was 12,400, with 76 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 21 per cent lymphocytes and 2 per cent monocytes. The pharyngitis cleared rapidly, and recovery was uneventful.

CASE 10.—C. R., a Negro woman aged 25, was admitted to the hospital on Aug. 8, 1944 with a diagnosis of early latent syphilis, not previously treated. She was given the twenty-five day treatment, receiving 55 mg. of oxophenarsine hydrochloride daily. On her admission the hemoglobin content was 60 per cent and the white blood cell count 6,000, with 65 per cent polymorphonuclear neutrophils, 33 per cent lymphocytes and 2 per cent monocytes. The urine was essentially normal.

The patient tolerated the drug well. A routine blood count performed after the twentieth dose of the drug showed a white blood cell count of 3,800, with no polymorphonuclear neutrophils, 2 per cent eosinophils, 58 per cent lymphocytes and 40 per cent monocytes. During the same evening there was a rise in the patient's temperature to 103 F. At the same time there were noted necrotic ulceration of the gingival tissue and a small eroded area on the right tonsil. Arsenotherapy was discontinued, and the patient was given liver intramuscularly, pentnucleotide and dimercaprol. During the following days there was a complete absence of granulocytes. On the third day after the institution of treatment for the agranulocytosis, granulocytes reappeared. The white blood cell count was 4,500, with 15 per cent polymorphonuclear neutrophils, 55 per cent lymphocytes and 30 per cent monocytes. Recovery was uneventful.

CASE 11.—O. D., a Negro girl aged 17, was admitted to the hospital on Aug. 11, 1944 with a diagnosis of early latent syphilis, not previously treated, and eight months' pregnancy. She was treated according to the twenty-five day schedule, receiving 60 mg. of oxophenarsine hydrochloride daily. On her admission the hemoglobin content was 75 per cent, and the white blood cell count was 7,200, with 55 per cent polymorphonuclear neutrophils, 43 per cent lymphocytes and 2 per cent monocytes. The urine was essentially normal.

The patient tolerated the drug well until the twentieth dose, at which time in a routine blood count it was noted that the white blood cell count had fallen to

3,500, with 5 per cent polymorphonuclear neutrophils, 3 per cent eosinophils, 59 per cent lymphocytes and 33 per cent monocytes. She had no complaints. Examination revealed only slight injection of the pharynx, and her temperature was 100.8 F. On the next day the hemoglobin content was 55 per cent and the white blood cell count 3,800, with a complete absence of granulocytes, 50 per cent lymphocytes and 50 per cent monocytes. Her temperature remained elevated for four days, reaching 101.3 F. The drug was withdrawn. On the second day of her reaction the patient went into labor and was delivered of a full term living infant. She was treated with pentnucleotide, liver extract intramuscularly and dimercaprol. She also received two blood transfusions (500 cc. each). Her temperature dropped by lysis after the fourth day. On the fifteenth day following the reaction, the hemoglobin content was 85 per cent, and the white blood cell count was 7,300, with 56 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 37 per cent lymphocytes and 5 per cent monocytes. The patient made an uneventful recovery.

CASE 12.—B. L., a Negro woman aged 20, was admitted to the hospital on June 3, 1944 with a diagnosis of early latent syphilis, previously treated, and gonorrheal cervicitis. She was treated according to the twenty-five day schedule, receiving 55 mg. of oxophenarsine hydrochloride daily. At the same time she was given 4 Gm. of sulfathiazole daily for five days. On her admission, the hemoglobin content was 77 per cent, and the white blood cell count was 6,500, with no differential count made. The urine was essentially normal.

The patient tolerated the drug well until the eighteenth injection; then she had a sore throat and chilly sensations and a temperature of 102.2 F. On examination there were diffuse redness and edema of the pharynx and ulceration of several areas on both tonsils. At this time the hemoglobin content was 80 per cent; the red blood cell count was 4,410,000, and the white blood cell count was 3,000, with a complete absence of granulocytes, 87 per cent lymphocytes and 13 per cent monocytes. Arsenotherapy was discontinued and treatment with pentnucleotide and dimercaprol instituted. Her temperature remained elevated for four days, reaching 103 F., after which it fell by lysis. Granulocytes reappeared within three days, at which time the hemoglobin content was 82 per cent, the red blood cell count 4,400,000 and the white blood cell count 4,000, with 90 per cent polymorphonuclear neutrophils, 1 per cent basophils, 4 per cent lymphocytes and 5 per cent monocytes. On the next day the white blood cell count was 6,600, with 24 per cent polymorphonuclear neutrophils, 68 per cent lymphocytes and 8 per cent monocytes. On the fifth day following the reaction the white blood cell count was 9,600, with 56 per cent polymorphonuclear neutrophils, 38 per cent lymphocytes and 6 per cent monocytes. The patient made an uneventful recovery.

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TINEA NIGRA

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LANGERON [1] has stated the belief that knowledge of the epidermomycoses with black pigmentation is still imperfect, for two reasons. The first is nomenclature, as the same disease has received different names according to the different countries and the several observers connected with the study of this morbid condition. It is also an undoubted fact that the same name has been given indiscriminately to different diseases. The second factor responsible for the prevailing confusion is that the fungi which cause this epidermomycosis are mostly unknown or imperfectly known, for they have not been carefully studied. For these reasons we have resolved to make the fullest possible study of this mycosis both from the anatomoclinical point of view and from the mycologic standpoint of its causal agent.

DEFINITION

Tinea nigra is a contagious, inoculable and autoinoculable dermatomycosis which is caused by two fungi, Cladosporium mansoni and Cladosporium wernecki. It is characterized, from the clinical point of view, by its black or brown coloration and by its sites of preference on the trunk and neck (Orient) and on the palmar region (Brazil and Cuba); the disease may, however, occur on any part of the cutaneous tegument.

HISTORY

The first reference to tinea nigra was made by Manson [2] in 1872, in south China. Manson's observations, however, were forgotten, especially as he made no reference to them in his subsequent works.

In 1905 Castellani [3] rediscovered the disease, in Ceylon, and isolated its causal agent. As regards the disease which Cerqueira [4] in 1891, in

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* From the Instituto Ezequiel Dias.

1. Langeron, M.: Tinea nigra et keratomycosis nigricans palmaris, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, pt. 2, p. 361.

2. Manson, P., cited by Castellani and Chalmers.[3]

(Footnotes continued on next page)

Bahia (Brazil), called keratomycosis nigricans palmar, his object was to individualize a morbid entity observed by him which produced a black coloration and was localized on the palms. Cerqueira's [4] work, however, did not become widely known in Brazil; it was only in 1916 that his son, Cerqueira Pinto,[5] made use of his father's observations and some of his own in his doctor's thesis, which attracted no great attention in the author's own country.

Silva [6] affirmed that in a report of Castellani and Chalmers [7] they verified, by examining the China Maritime Custom House Medical Reports, that the disease described by Manson [2] was not tinea nigra but was perhaps tyriasis versicolor. If this is so, then Cerqueira [4] was the pioneer in the study of this mycosis.

In 1921 Ramos e Silva,[8] in Rio de Janeiro, reported another case, in which Parreiras Horta [9] isolated a fungus that he called C. wernecki, after Prof. Werneck Machado, a Brazilian dermatologist.

Later, in 1929, 1930, 1932 and 1935, Silva [10] observed new cases in the state of Bahia, where also Silva and Mendonça[10c] in 1932 reported a case, as also did de Aguiar [11] in 1937.

Da Fonseca and Ferreira da Rosa [12] stated that up to 1930 at least 26 cases were reported in Brazil. There is no record of the occurrence of tinea nigra in the other states of Brazil. Pardo Castelló [13] in 1938 reported and gave an excellent description of a case in Cuba. The first case in Minas Geraes was reported by one of us (O. G. Costa)

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3. Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, ed. 3, London, Ballière, Tindall & Cox, 1919, p. 2078.

4. Cerqueira, A., cited by Cerqueira Pinto.[5]

5. Cerqueira Pinto, G. C.: Keratomycose nigricans palmaris, Thesis, Bahia, Brazil, 1916.

6. Silva, F.: Keratose nigricans (Alexandre Cerqueira, 1891); Tinea nigra (Castellani, 1905), Ann. de dermat. et syph. **6**:928-936, 1935.

7. Castellani and Chalmers, cited by Silva.[6]

8. Ramos e Silva, cited by Silva.[6]

9. Parreiras Horta, P.: Sobre un caso interessante de tinea nigra, Rev. med.-cir. do Brasil **29**:269-274, 1921.

10. (*a*) Silva, F.: Tinea nigra (Cladosporiose epidermica), Brasil-med. **43**:924-926, 1929; Sobre un caso de tinha preta e un novo cogumelo An. brasil. de dermat. e sif. **5**:9-16, 1929; (*b*) A proposito da "tinea nigra" (kerato-mycosis nigricans palmaris), Brasil-med. **44**:1201-1204, 1930. (*c*) Silva, F., and Mendonca, B.: An Interesting Case of Tinea Nigra, Gac. med. da Bahia, 1932, p. 591. (*d*) Silva.[6]

11. de Aguiar, C: Um caso interessante de "ceratomicose nigricans palmar" ou "tinea nigra," Bahia med. **8**:137-140, 1937.

12. da Fonseca, O., and Ferreira da Rosa, A.: On a Case of Keratomycosis Nigricans Palmaris, Rev. med.-cir. do Brasil **38**:341-344, 1930.

13. Pardo Castelló, V.: Keratomycosis nigricans palmaris, Rev. argent. de dermatosif. **22**:255-264, 1938.

and forms the subject of this paper. Unfortunately, through circumstances over which we had no control, we were unable to see the papers of Silva and Mendonça,[10c] Pinoy,[14] Castellani,[15] Sartory, Sartory and Meyer [16] or Sartory, Sartory, Meyer and Weiss.[17]

SYNONYMS

Tinea nigra is also known as keratomycosis, keratomycosis nigricans palmaris, cladosporiosis epidermica, pityriasis nigra and microsporosis nigra. The denominations keratomycosis or ceratomycosis nigricans palmaris should not be adopted, because there are extrapalmar localizations of the disease, to be met with in the East and even in Brazil.

Besides this, the term keratomycosis may cause confusion with corneal ocular mycoses. The most suitable name would be cladosporiosis epidermica, but this name is inconvenient, as it refers to the causal agent, which may in the future receive a different mycologic classification.

The name pityriasis nigra is unsuitable for two reasons: first, because it is liable to be confused with pityriasis versicolor and, second, because the name pityriasis should be limited to the cutaneous diseases in which desquamation is a primary manifestation, and this is by no means the case in the disease we are studying.

The name microsporosis is self condemning, as this is a mycosis caused not by a microsporum but by a cladosporium.

For these reasons we are of the opinion that, both for the oriental and for the occidental mycoses, the original name of tinea nigra should be conserved; this name, while not subordinated to topologic or etiologic considerations, satisfies all the conditions of a chronologic and chromatic order (cutaneous lesions and aspect of the cultures of the parasite) and describes a superficial cutaneous manifestation, as the tineas generally are.

GEOGRAPHIC DISTRIBUTION

The disease is confined to the East and to the American continent. In the East it has been reported from Ceylon, India, Burma, south China, Java, Sumatra and Bangka, Timor and Borneo. In Brazil it has been met with in the states of Bahia, Rio de Janeiro and Minas Geraes. Pardo Castelló [13] has reported a case in Cuba.

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14. Pinoy, E.: Ann. de dermat. et syph. **3**:341-343, 1912.

15. Castellani, A.: Tropical Dermatology, International Conference on Health Problems in Tropical America, 1924.

16. Sartory, A.; Sartory, R., and Meyer, J.: Tinea Nigra, Rev. prat. d. mal. d. pays chauds **17**:557-576, 1937.

17. Sartory, A.; Sartory, R.; Meyer, J., and Weiss, R.: Etude d'un "Cladosporium" nouveau "Cladosporium tropicalis" n. sp. isolé d'une dermatomycose tropicale, Bull. Acad. de méd., Paris **113**:890-892, 1935.

CLINICAL SYMPTOMS

The clinical symptoms of tinea nigra are nearly identical in the Western and Eastern hemispheres. In the East the favorite sites are the neck and upper part of the thorax; the disease, however, may affect any part of the integument, the face being the least often affected. In the Western hemisphere, the disease in the great majority of cases is found in the palmar regions. The palmar site is so common in Brazil that in 1930 Rietmann,[18] rediscovering the disease, expressed the opinion that the palmar site was the only site, affirming that this dermatomycosis occurs exclusively on the palms, that is, on the thenar and hypothenar regions and on the concavity of the hand, but that it could in extensive eruption sometimes affect the palmar surface of the first phalanges but never spread beyond the edge of the fingers. The soles, like the other parts of the tegument, are unaffected. There is no modification of sweating in the palmar regions.

Silva [6] affirmed that the most frequent sites in cases in Brazil are the palms, the sides of the fingers, the wrists, the interdigital spaces and the cubital border. De Aguiar [11] has reported cases of the eruption occurring on the dorsum of the hand and fingers. Ramos e Silva [19] saw a case in which the disease occurred on the neck of a physician.

In the East, Castellani and Chalmers [7] saw a patient in whom the dermatomycosis affected the palm of the left hand. Silva [6] referred to doubtful lesions of the nails and to localization on the neck.

The disease is manifested by the appearance of black or brown spots. The primary lesions coalesce, later forming irregular polycylic patches of varying size, which are smooth and slightly or not at all itchy, with moderately raised edges. Neither erythema nor any inflammatory phenomenon is noticed. Brazilian authors have stated that the patches are smooth, with ill defined borders, the edges are not raised and there is no itching. Pardo Castelló [13] made a good comparison between the color of tinea nigra and that of india ink.

Rietmann [18] stated that no scales, vesicles or raised edges are observed, the patches being absolutely level but at times rough to the touch. Silva was of the opinion that the patches fade or disappear spontaneously, to reappear and increase later.

Arêa Leão, Cury and Ferreira Filho [20] stated:

When the patinet washes his hands frequently the lesions fade away, while if there is insufficient cleanliness there is more humidity and grease in the skin and the

18. Rietmann, M. B.: Note préliminaire sur une épidermomycose palmaire noire observée dans l'état de Bahia au Brésil, Bull. Soc. franç. de dermat. et syph. **37**:202-207, 1930.

19. Ramos e Silva, J.: Sobre un nova caso de tinea nigra, Brasil-med. **44**:755-757, 1930.

lesions have a tendency to increase, as the mold then finds more favorable conditions for its development. The preference of the mold for the palmar and not for the dorsal region of the hands and the absence of the disease from other moist and greasy sections of the skin are a peculiarity that has not yet been explained.

COMPARATIVE PATHOLOGIC CHANGES OF ORIENTAL TINEA NIGRA AND SO-CALLED KERATOMYCOSIS NIGRICANS PALMARIS OF THE WESTERN HEMISPHERE

Langeron and Horta [21] expressed the opinion that the parasites of oriental tinea nigra and so-called keratosis nigricans palmaris are different, their opinion being based on the appearance of the parasites in the scales and in cultures.

In Brazil, Silva [6] was first to admit the clinical identity of the two mycoses; his opinion was expressed as follows:

1. The fungus responsible for tinea nigra belongs to the genus Cladosporium (Cladosporium mansoni: Castellani, 1905).

The fungus isolated in Brazil by P. Horta (Cladosporium wernecki: Horta, 1921) and that isolated by Sartory, Meyer and Rietmann belong to the same genus.

2. The aspect of the dermatosis is the same in Ceylon, in Java, in Burma, in Malaya, in Bahia or in Rio de Janeiro (Brazil); the differences which exist refer exclusively to sites of election.

The oriental mycosis is localized preferentially on the neck and upper part of the thorax, while the American form of the disease nearly always attacks the palmar regions and the palmar surface of the fingers. It must be pointed out, however, that in Ceylon Castellani [22] observed palmar localization while in Brazil Ramos e Silva [19] and Silva [6] have observed eruptions affecting the neck.

Langeron [1] stated the belief that the two diseases are different, because tinea nigra of the palms seems to be an exclusively tropical or even exclusively Brazilian disease, occurring generally on the palms and rarely on other parts of the skin. There is also the fact that the type of cladosporium which is the causal agent is different from that which produces tinea nigra.

Langeron [1] therefore concluded that the two epidermomycoses are definitely differentiated by their clinical, geographic and etiologic features. As regards localization, we have seen that both dermatoses may affect the hands and the neck indifferently. As regards geographic distribution, it has been shown that both diseases are met with in tropical

20. Arêa Leão, A. E.; Cury, A., and Ferreira Filho, J. M.: Tinea Nigra (Keratomycosis Nigricans Palmaris): Observation and Study of a Case, Rev. brasil. de biol. **5**:165-177, 1945.

21. Langeron, M., and Parreiras Horta, P.: Note complémentaire sur le cladosporium Wernecki-Horta, 1921, Bull. Soc. path. exot. **15**:381-383, 1922.

22. Castellani, A., cited by Silva.[6]

or subtropical regions. As regards the parasites, these differ only in species, for both belong to the genus Cladosporium.

Our belief being based on these facts, we are of the same opinion as Silva,[6] viz., that the two diseases are identical. We can cite the example of other mycoses, e. g., sporotrichosis and actinomycosis, whose causal fungi belong to different species; we describe them, however, under the same name, though they may assume a special clinical aspect, as happens with sporotrichosis in Brazil.

ETIOLOGY

Tinea nigra is caused by the action of C. mansoni in the East and by C. wernecki in the Americas. This disease seems to be peculiar to tropical or subtropical countries. The color of the skin does not seem to exercise any influence, for in Brazil it is met with in white persons, mulattoes and Negroes, though most frequently in white persons. The ages most frequently attacked are from 16 to 60. The disease affects both sexes indifferently. Contagión from one person to another has been reported more than once. Some cases of family contagion have also been registered. The disease has been transmitted experimentally to human beings and guinea pigs. Arêa Leão, Cury and Ferreira Filho [20] have tried to reproduce the disease in human beings and in animals (guinea pigs, rabbits and rats), without results. In the East this disease attacks natives by preference. It has been noticed that this dermatomycosis affects the upper classes more frequently, which is contrary to the general rule. In the majority of cases tinea nigra bears no relation to the professional activities of the patient or to his animal or vegetable contacts.

Pardo Castelló [18] related that in his case the patient said that he had had a fall in the garden and slightly bruised the skin of the left hand; two weeks later there appeared a black punctiform patch. We believe this to be the first reference to the period of incubation of the disease and to the solution of continuity of the cutaneous surface which allowed of the possible penetration of the fungus.

MYCOLOGIC STUDY

It is easy to isolate the causal agent of tinea nigra from the scales scraped from the cutaneous lesion; all authors are unanimous on this point. In the same way it was extremely easy for us to isolate from the palmar lesion of M.A.N.C. the fungus which we shall now describe.

Macroscopic and Microscopic Aspects of the Cultures.—1. Sabouraud's Maltose Agar: On the third day we noted in the scales on the surface of the substratum near the tube wall the appearance on microscopic examination (eyepiece 4, objective B, Zeiss microscope) of the first hyphae leaving the scales and invading the medium. On the fourth

day the first ramifications appeared; these were dichotomous or formed acute angles, wider or narrower, or right angles; septum formation was already well defined. On the fifth day there appeared macroscopically small dark points in the scattered scales, while in the colonies mentioned the branchings became more numerous as development proceeded. On the sixth day there was already noted macroscopically the appearance of small, dark, more spherical colonies; these had a rounded outline and measured 0.5 mm. at most. On the eleventh day the colonies measured 2 to 4 mm. in diameter and were more or less circular in outline; some of these had a mamiliform central spot, dull greenish black,

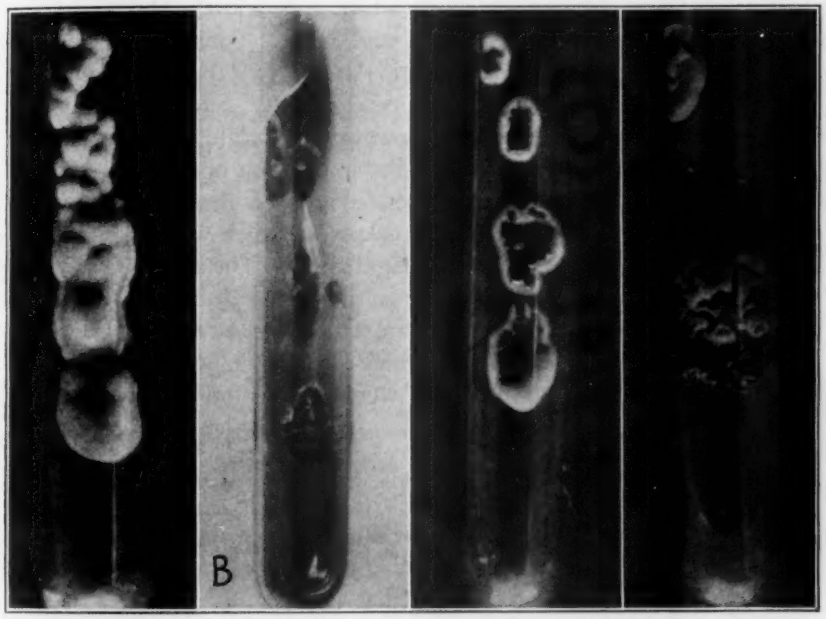

Fig 1.—Cladosporium wernecki. *A*, culture of cespitose type, nine days, in Sabouraud's maltose-agar medium. *B*, culture of glabrous type, nine days, in Sabouraud's maltose medium. *C*, mixed type culture (glabrocespitose, nine days, in Sabouraud's maltose-agar medium). *D*, culture, seventy-four days, in Sabouraud's maltose agar. Note the absorption of the down.

surrounded by a border of short, velvety, grayish green hairs measuring sometimes 1 mm. in width. In other colonies the central zone was wider, black, shining, smooth and moist, with mamillae separated by grooves; there was the same border previously described, of the same color and aspect but extremely narrow. On the twenty-third day some colonies measured 1.4 cm. in diameter, with a central umbilication measuring 0.1 cm. in diameter and of a slightly greenish gray. This was followed by another, which was dark gray, glabrous, 0.3 to 0.4 cm.

in diameter with a border of the same color as the central zone, filamentous, satiny looking, 0.15 to 0.2 cm. in width and free from radiations. Such colonies we shall term cespitose (fig. 1 *A*). Other colonies showed a central black umbilication, smooth and brilliant, surrounded by a zone measuring about 0.4 cm. in width and filamentous in aspect. Outside this there was another border, 0.25 to 0.15 cm. in width, rather dark and almost glabrous. These we shall call glabrous colonies (fig. 1 *B*). In the former type filamentous forms were predominant, while in the latter the yeast forms were commonest. These data refer to cultures made from scales. Da Fonseca and da Rosa [12] stated that in Sabouraud's maltose medium the cultures show only greenish brown yeast forms; our cultures, however, which were closely observed from the start, contained simple hyphae and ramifications, with complete absence, at least with the magnification indicated (that is, eyepiece 4, objective B, Zeiss microscope), of yeast forms. Such forms appear from the fourth to the sixth day, however, as isolated islets in certain parts of the scattered scales, giving the impression of a mixed culture. To exclude this hypothesis we suspended in 0.85 per cent solution of sodium chloride a small portion of a colony in which we had seen yeast forms under the microscope on the eighth day. The results confirmed our suspicion, for we were able, after cultivation on Sabouraud's maltose medium, to separate in an almost pure state the two cultural types, that is, the glabrous type (fig. 1 *B*), in which yeast forms were predominant, and the cespitose type (fig. 1 *A*), in which filamentous forms prevailed.

Cultures on Corn Meal Agar (Emmons' [23] method): In a medium of corn meal agar also the two types can be separated, one glabrous and the other cespitose.

1. The colonies look smooth, black and somewhat shining and are surrounded by short mycelial grayish filaments. They secrete a dark pigment, varying from Saccardo's umber (Ridgway,[24] plate XXIX, 17″ O-Y.*k*) to sepia (plate XXIX, 17″ O-Y.*m*), which is intensely diffused throughout the medium.

2. The colonies are lighter in color, deep olive (plate XL, 21‴ O-YY. *k*) in the central part and surrounded by a finely radiated border, dark yellowish olive in color (plate XL, 21‴ O-YY.); only traces of yellowish olive pigment (plate XL, 21‴ O-YY.*d*) are diffused in the medium.

Figure 1 *C* represents a culture of mixed type, that is, glabrous-cespitose, in Sabouraud's maltose medium.

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23. Emmons, C. W.: Observations on Achorion Gypseum, Mycologia **23**:87-95, 1931.

24. Ridgway, R.: Color Standards and Color Nomenclature, Washington, D. C., The Author, 1913.

CLASSIFICATION OF THE CAUSAL AGENT

Dodge [25] and Negroni [26] classified the causal agents of the two forms of tinea nigra—the American and the Asiatic—as belonging to the genus Dematium Persoon, 1794; Langeron [27] and Brumpt [28] classified the agent of Asiatic tinea nigra as genus Torula Persoon, 1796, while Pinoy,[14] in 1912, classified it as Cladosporium Link, 1816. In spite of this, Langeron [1] and Brumpt [28] classified the agent of American tinea nigra as Cladosporium. These divergencies are related probably to the forms present in the cultures of the fungus which would specially draw the attention of these mycologists. We think that it would not be inopportune to transcribe here the generic diagnoses referred to. Engler and Prantl [29] stated:

Dematium Pers. (*Sporodum* Corda, *Conoplea* Pers.). *Hyphen kriechend, wenig entwickelt oder auch rasige Lager bildend. Conidienträger aufrecht, unverzweigt oder spärlich verzweigt, septiert, seitlich Conidienketten tragend Conidien kugelig oder eiförmig, bisweilen durch kurze Zwischenstüke verbunden, einzellig, dunkel gefärbt.*

Torula Pers. (*Tetrocolium* Link). *Hyphen niederliegend. Conidientragende Äste sehr kurz oder kaum von den Conidien verschieden. Conidien in Ketten gebildet, einzeln oder in Verbänden sich loslösend, einzellig, dunkel bis schwarz, kugelig bis länglich, glatt oder rauh.*

Cladosporium Link. *Hyphen kriechend, septiert, auf der Oberfläche oder im Substrat. Conidienträger fast aufrecht, verzweigt und verflochten, oft rasenbildend, olivenfarben. Conidien kugelig und eiförmig, zuerst ungeteilt, dann meist mit einer Scheidewand, meist auch grünlich gefärbt, endständig und dann zur Seite gedrängt (sympodialer Conidienstand).*

From the aforementioned statements, we deduce that Dodge [25] and Negroni [26] were impressed by the conidial system, that is, spherical or ovoid conidia, which are unicellular, dark colored and sometimes joined by short, intermediate elements; Langeron [27] and Brumpt,[28] however, were impressed by the conidium-bearing branches which are short or just distinguishable from the conidia. These chain forms occur isolated or in groups, unicellular, dark and even black, spherical or elongated and smooth or rough. Pinoy [14] was impressed by the conidiophores, almost erect, branched and interlaced, frequently cespitose and olive colored. Spherical or ovoid conidia at first are not subdivided,

25. Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, pp. 676-678.

26. Negroni, P.: Dermatomicosis: Diagnostico y tratamiento, Buenos Aires, Aniceto Lopez, 1942, p. 811.

27. Langeron, M., cited by Brumpt.[28]

28. Brumpt, E.: Précis de parasitologie, Paris, Masson & Cie, 1936, pt. 2, p. 1791.

29. Engler, A., and Prantl, K.: Die natürlichen Pflanzenfamilien, Leipzig, Wilhelm Engelmann, 1900, pt. 1, no. 1 * *, pp. 458, 459 and 475.

but, later, subdivisions occur in greater proportion, with a septum, generally greenish, acrogenous and later pleurogenous (sympodial conidial stage).

In general, all these generic data indicative of the species are represented in these two fungi which cause tinea nigra; they occur and may vary with the age of the cultures or according to the moment when the cultures are examined and according to the region from which the fragment was taken for examination, whether from the center, periphery or intermediate zone. These are all facts well known to mycologists, and there are others which it would be tiresome to mention.

We have had the opportunity, however, of comparing preparations of C. mansoni and of C. wernecki, and we were able to conclude that there is a specific difference between the two fungi. In the former, as a matter of fact, in the conidial apparatus, besides the predominant fuliginous spherical forms there are ovoid hyaline forms which, in our opinion, are the youngest forms. Among the predominant forms there are some with a rough outer surface and others with one septum of a more or less fuliginous color and of varying dimensions (3.5 by 2.0 microns or 7.0 to 8.5 microns by 2.0 or 2.5 microns).

Pollacci and Nannizzi [30] stated that C. mansoni, "examined under the microscope, is seen to consist of a dense interlaced mass of brown hyphae, with short segments, of varying shape, frequently oval or round and divided sometimes into spherical arthrospores 8 to 10 microns in diameter containing generally a large oily drop of liquid. More rarely on the surface of the colonies, especially in adult ones, there appear olive-colored hyphae, with few ramifications, some 0.8 to 1 micron and sterile and others 2 to 2.5 microns wide and terminated by oval or elliptic conidia."

The preparation which we had the opportunity of examining accompanies the volume referred to, that is, that of Pollacci and Nannizzi.[30] For comparison we used a preparation made from a culture obtained from scales of the lesion of M.A.N.C., 15 days old. In this preparation there was a predominance of oval or elliptic conidia of an intense olive-fuliginous color; some of them are hyalin, the spherically shaped being less abundant. Among the former there are some with a rough outer surface; they have mostly one septum, but some have two or three septums, of variable dimensions: length 2.9 to 13.0 microns (average 6.36 microns) and width 1.4 to 5.8 microns (average 3.47 microns). There was the same constitution when examined under the microscope, that is, densely interlaced, brown, fuliginous hyphae with short segments, sometimes elongated, rounded or oval dividing

30. Pollacci, G., and Nannizzi, A.: I miceti patogeni d'ell uomo e degli animali, Bologna, L. Cappelli, 1928, pt. 7-8, p. 62.

into the same kind of arthrospores seen in C. mansoni and measuring 2.9 to 11.6 (average 8.45) microns by 5.8 to 11.6 (average 8.14) microns; on the surface of the colonies there often appear olive-colored hyphae sometimes with ramifications, varying in number, sterile, 0.7 to 1.4 microns and others 2.9 to 5.8 microns in width, terminating in conidia as mentioned.

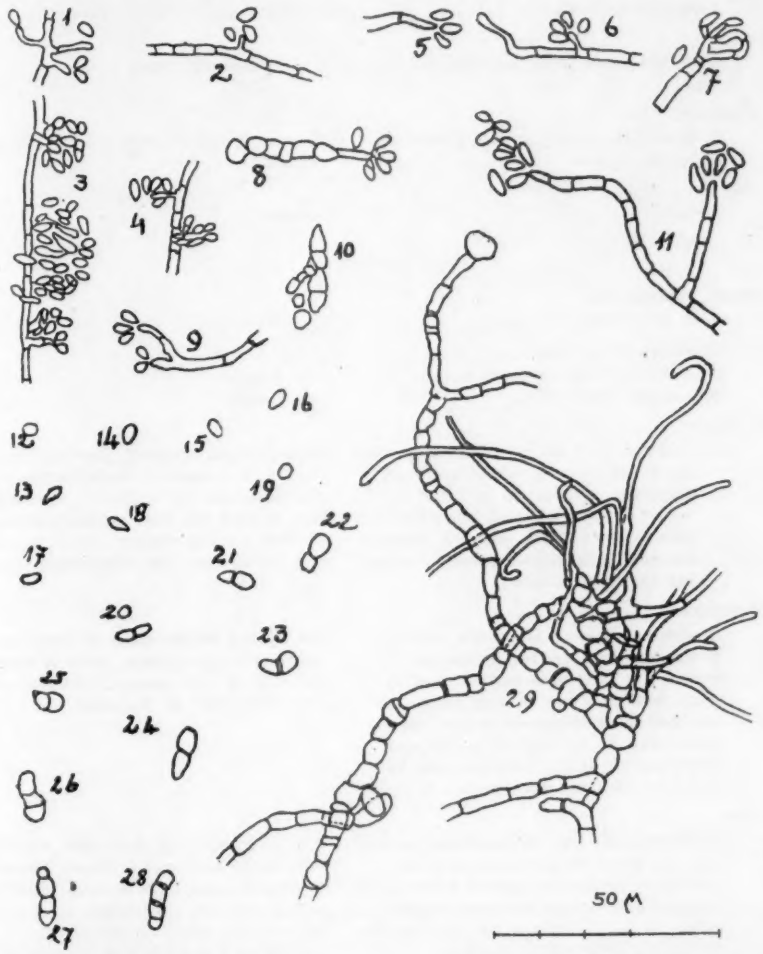

Fig. 2.—Cladosporium wernecki. *1* to *4*, various aspects of conidiophores observed in culture on cover slip in Sabouraud's maltose medium on tenth day. *5* to *11*, conidiophores in cultures twenty-six days old dissociated in Ammann's lacto-phenol. *12* to *28*, conidia in their various forms.. *29*, aspect of mycelium corresponding to glabrous cultures.

By the foregoing description it will be seen that while there are generic characters which are comparable there are, however, certain specific differences which justify us in considering them as distinct species and so maintaining them mycologically.

Comparison of Cladosporium Wernecki with Cladosporium Mansoni

	Cladosporium Wernecki, Parreiras Horta, 1921	Cladosporium Mansoni, Pinoy, 1912 (According to Pollacci and Nannizzi and Colleagues)
	In the Lesions	
Mycelial articles	32.0 to 116.6 (average 32.0) by 1.4 to 2.97 (average 2.9) microns, simple or branched	18 to 20 by 2.5 to 3.5 microns, not branched
Color	Fuliginous or hyaline	Fuliginous
Spores	4.0 to 8.7 (average 5.8) microns, round or ovoid	5 to 10 microns, round
Arrangement	In groups, branched or not, pigmented or hyalin, curved	In groups, unbranched, curved like a banana
Outline	Irregular	Irregular
	Cultures	
Optimum temperature	18 to 25 C. (surroundings)	30 to 32 C.
First appearance of colonies		
Macroscopic:	fifth to sixth days	2 to 4 days
Microscopic:	third day	2 to 4 days
Two types	1. Hemispherical colonies, doughy, shining black, nonadherent to medium 2. Cespitose, olive-gray, strongly adherent to medium; both when they become old get dull, with an irregular smooth black surface strongly adherent to the substratum	Hemispherical, rounded, greenish, then black with greenish delicate fibrillae irradiating toward the periphery; these are at first isolated but later become confluent to form a black shining plaque, penetrating deeply into the substratum
Microscopically	Predominance of yeast forms (conidia) in the first type and of hyphae in the second; the latter are septate, now in short segments, now in long ones, arranged in arthrospores or not. the external wall of the surface rough and measuring 2.9 to 11.6 (average 8.45) by 5.8 to 11.6 (average 8.14) microns in length	The hyphae are brown, with short segments of varying shape, oval or round and divided into spherical arthrospores 8 to 10 microns in diameter
Conidia	Oval or elliptic ones predominate; rarely they are spherical, fuliginous or hyalin, nonseptate or having up to 3 septums, the uniseptate being predominant; dimensions; 2.9 to 13 (average 6.36) microns by 1.4 to 5.8 (average 3.47) microns	The spherical fuliginous types predominate, ovoid and hyalin; among the first mentioned some have a rough external wall, a few are uniseptated, of a more intense olive color; dimensions: 3.5 to 2 microns or 7 to 8.5 or 2 to 2.5 microns
Hyphae	Sterile, measuring 0.7 to 1.4 microns in width	Sterile forms, 0.8 to 1.0 micron wide
	Fruitful, 2.9 to 5.8 microns in width	Fructifying forms, 2 to 2.5 microns wide
Type of fructification	Acrogenous and pleurogenous (sympodial)	Acrogenous and pleurogenous (sympodial ?)

The accompanying table contains a summary of these differences not only from the clinical point of view but also from the mycologic standpoint.

The sample of C. wernecki isolated and studied by us in no way differs from the samples studied by Parreiras Horta,[9] Langeron,[1] Pardo Castelló,[18] Arêa Leão and colleagues,[20] Fonseca Filho and Ferreira da Rosa,[12] Flaviano Silva,[6] Sartory, Sartory, Rietmann and Meyer [31] and

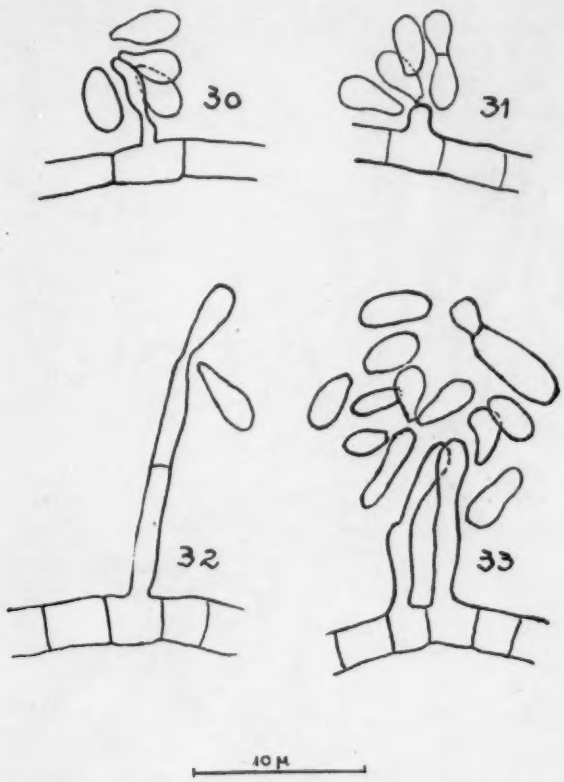

Fig. 3.—Cladosporium wernecki. Conidiophores, ten days, in culture on cover slip in Sabouraud's maltose medium.

others except that in our case we obtained and isolated two distinct cultural types already mentioned by various authors—the cespitose and the glabrous.

As regards the microscopic appearance, we have mentioned in this paper the various aspects of the conidiophores (figs. 2 and 3) which we observed in microcultures on cover slips after treatment with Ammann's lactophenol or staining with ferric hematoxylin by

31. Sartory, A.; Sartory, R.; Reitmann, B., and Meyer, J.: Contribution à l'étude d'une épidermomycose brésilienne palmaire noire, provoquée par un cladosporium nouveau, Compt. rend. Soc. de biol. **104**:878-881, 1930.

Heidenhain's method. This preparation was made in order to study the cytology of the fungus, which is as follows.

CYTOLOGY OF C. WERNECKI

The mycelial cells, whose cytoplasm is of variable structure, are uninuclear, the nucleus being situated in irregular fashion, sometimes

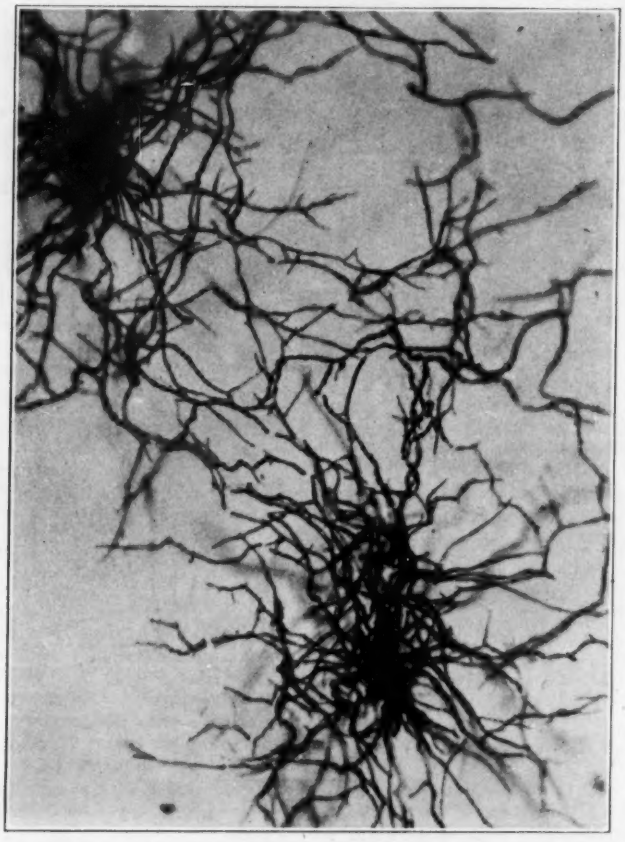

Fig. 4.—Cladosporium wernecki. Mycelial aspect of Hormiscium type. Stained with iron hematoxylin × 233.

centrally, sometimes laterally near the hyphae wall and sometimes at one of the extremities. It consists of a strongly siderophilous karyosome, which is homogeneous or nearly homogeneous and surrounded by a delicate membrane made up of fine chromatin granulations, and between this membrane and the karyosome there are frequently seen fine siderophilous granules. Sometimes a narrow hyaline zone is seen around the karyosome. In some cells which resemble spores of the Alternaria type we have sometimes noticed the presence of four nuclei, which are at times well differentiated.

The septation of the hyphae may vary, according to the cultural type; sometimes the segments are short, recalling the Hormiscium (fig. 4) type, especially in glabrous cultures; at other times the segments are longer in cultures of the cespitose or filamentous types. This cytologic study was undertaken by us to see whether we could discover an explanation for the morphologic instability of C. wernecki. Is this instability due to the phenomenon of heterokaryosis so deeply studied by Hansen and Smith [32]? We are of the opinion that the cytologic data obtained by us do not furnish the necessary explanation and therefore that the cultural variability of C. wernecki is not based on heterokaryosis. The polymorphism of the genus Cladosporium is great, and Berlese [33] has already pointed to it, as a result of his studies of isolated samples. This fact has, as we have seen, made classification difficult.

Our studies have enabled us not only to confirm the conclusion of the majority of authors but also to adduce new facts which lead us to place the causal agents of tinea nigra in the genus Cladosporium.

In view of the foregoing we conclude that the causal agent of American tinea nigra should be considered as belonging to the genus Cladosporium and that the species C. wernecki Parreiras Horta, 1921, is legitimate, having the following synonyms:

Montoyella nigra, Castellani and Chalmers, 1913
Cladosporium sp., Rietmann, 1930
Cardosporium sp., Sartory, Sartory, Rietmann and Meyer, 1930
Dematium wernecki, Dodge, 1935
Cladosporium Rietmann, Sartory, 1935
Cladosporium tropicalis, Sartory, Sartory, Meyer and Weiss, 1935

We believe that we have in this way contributed toward clearing up one of the points of confusion so commonly found in the realms of mycology.

Dodge [25] stated the belief that the black form of caraté, pinta or kcara, seen in certain South American countries, is identical with tinea nigra, and at the end of page 576 in his "Medical Mycology," Dodge described Dematium wernecki (Parreiras Horta): "The organism usually isolated from black caraté, pinta or kcara in South America." This condition now has been proved to be due to treponema, its specific agent being Treponema carateum Brumpt, 1939.

POSITIVE DIAGNOSIS

Positive diagnosis is not difficult. The sites of election of the disease and its classic color, along with direct (40 per cent caustic soda or

32. Hansen, H. N., and Smith, R. E.: The Mechanism of Variation in Imperfecti Fungi, Botrytis Cinerea, Phytopath. **22**:953-964, 1932.

33. Berlese, A. N.: Première contribution à l'étude de la morphologie et de la biologie de cladosporium et dematium, Bull. Soc. mycol. France **11**:34-74, 1895.

Ammann's liquid) or cultural (Sabouraud's medium) tests will elucidate all cases.

DIFFERENTIAL DIAGNOSIS

The disease must be differentiated from pityriasis versicolor, epidermic blastomycosis, pinta or caraté (rare in Brazil), tinea nigrocircinata (Trichophyton ceylonense), chloasma, liver spots, melanoderma of Addison's disease and dermatitis due to Ficus caricaca (fig tree).

PROGNOSIS

The prognosis is favorable, for when proper treatment is given the mycosis disappears completely.

PROPHYLAXIS

Prophylaxis consists in suppression of the sources of contagion by early treatment and by disinfection of cutaneous wounds with tincture of iodine.

EVOLUTION

The evolution is benign, as the disease does not have any harmful consequences. There are no subjective symptoms. The patient does not notice his dermatosis, as it does not cause itching. A doctor is consulted more for esthetic reasons, when the plaque becomes larger and darker.

TREATMENT

Treatment is not difficult, for conditions in all cases yield to treatment.

Castellani [8] expressed the opinion that this mycosis is easily cured except when it is localized on the palms, when the treatment needs to be more prolonged.

Da Fonseca and Ferreira da Rosa [12] stated that if treatment is not adequately prolonged the disease recurs.

Silva [6] stated that he cured all his patients with an ointment composed of salicylic acid, benzoic acid, sulphur, resorcinol and petrolatum.

Our patient was radically cured by use of the following formula:

Metallic iodine	1 part
90 per cent alcohol	100 parts
Salicylic acid	1 part

The following formula is also recommended: 2 to 3 per cent alcoholic solution of salicylic acid and 10 to 20 per cent ointment of benzoic acid, sulphur and resorcinol.

REPORT OF A CASE

M. A. N. C. was a single girl, Brazilian domestic servant, aged 18, born at Dores da Boa Esperança (state of Minas Geraes). The family and personal history were of no interest. The patient consulted one of us (O. G. Costa) for a spot on the left palm.

Concerning the history of the present disease, the patient stated that about six months ago there appeared on her left palm brown spots, which increased until they attained their present size.

Fig. 5.—Tinea nigra. View of palmar lesion.

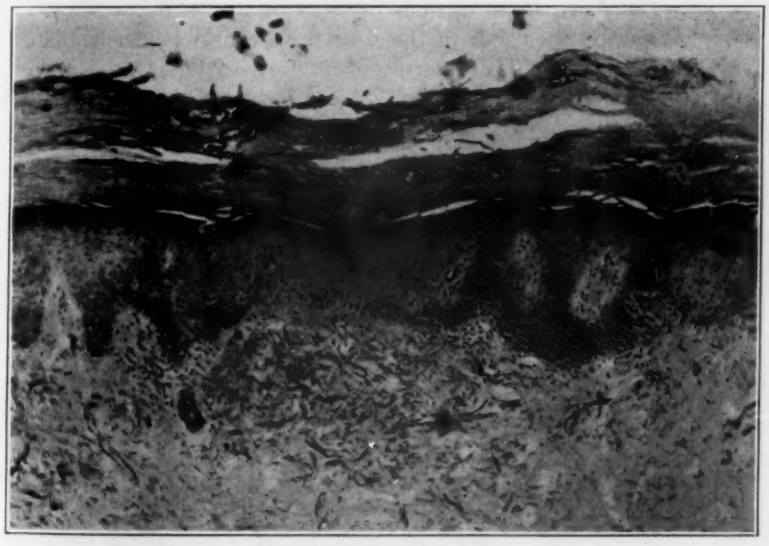

Fig. 6.—Tinea nigra. Histopathologic aspect of the palmar lesion.

The general examination showed nothing abnormal. The dermatologic examination showed several dark brown spots, some of which were punctiform and discrete and others confluent and more extensive. The edges of these spots were not raised

but were darker than the central parts, which in some cases were paler. The spots were not raised or itchy, and there was no scaling of any kind. There were no inflammatory symptoms. The dermatosis was confined to the palmar surface of the left hand (fig. 5).

Laboratory Examination.—The direct and cultural tests for C. wernecki (made by J. A. N.) elicited positive reactions.

Pathologic Examination.—We believe that no anatomopathologic study has been made of tinea nigra, and so we took from our patient a specimen for biopsy. This was sent to Dr. Moacir A. Junqueira, who supplied us with the following report:

"The fragment of skin had a thick corneal layer at the level of the more superficial strata, in which were seen mycelial fragments and spores of a light brown color; the hyphae were short, thick and septate and straight or curved, a terminal spore being seen in some of them. The presence of the fungus had brought about cleavage of the corneal layers. At times some filaments were met with deeper in the corneal layer, but not as deep as the stratum lucidum. In one of the sections examined there was seen a small area of parakeratosis, in which, however, no fungi were met. There were no modifications in the other epidermal layers. The changes met with in the derma were slight; at the level of the papillary body two small foci of lymphocytic infiltration were seen, and there was an increase of connective tissue cells (fig. 6) round an arteriole in the middle derma."

SUMMARY

We have described a case of tinea nigra which is the first recorded in the state of Minas Geraes, Brazil, by one of us (O. G. Costa).

Basing our conclusions on the clinical and mycologic study of this epidermomycosis, we consider that the name tinea nigra should be chosen, that the causal agent of the disease in the Western hemisphere is C. wernecki and that the eastern and western varieties should not be separated from the clinical point of view but only, and solely, from the point of view of the causal agents, which are the fungi C. mansoni and C. wernecki respectively.

Rua Ceará, 1691.

CHRONIC LATENT ORAL MONILIASIS (THRUSH)

Report of a Case of Twelve Years' Duration in Which the Disease Was Resistant to Treatment

SAUL S. ROBINSON, M.D.
AND
SAMUEL TASKER, M.D.
LOS ANGELES

MONILIAL infection of the mouth, or thrush, is common in infants and is occasionally observed in children and adults. The disease usually responds readily to local treatment and proper oral hygiene and cleanliness. There are, however, instances of oral thrush of a chronic latent type, resistant to all known therapy. A recent survey of twelve large dermatologic clinics [1] in the United States indicates that the chronic latent form of the disease is constantly encountered in dermatologic practice. The paucity of case reports in the medical literature and the omission of mention of the disease in this form in most dermatologic textbooks apparently indicate that chronic latent oral thrush has received little or no attention. It is the purpose of this article, therefore, to call attention to the resistant latent type of chronic oral moniliasis by reporting a case of twelve years' duration.

REPORT OF A CASE

H. S., a 7 year old girl of Jewish parentage, was first seen, on March 10, 1938, because of persistent white flaky lesions in the mouth and on the lips. The child was born at full term, by normal delivery and with an average birth weight. She was apparently free of lesions until the age of 2 years. The white patches first appeared on the tongue and then spread to the gums, the lips and the inner surfaces of the cheeks. All treatment prescribed for the disease during a period of five years had been ineffective. The girl was otherwise in good health and did not suffer from diarrheal or gastrointestinal disease. Her growth and her mental and physical development had been normal. She was able to take nourishment without difficulty except when the whitish flakes in the mouth became detached and left underlying raw, painful, bleeding surfaces. The child's mother was found to have oral and vaginal thrush at the time of the examination.

From the Department of Dermatology and Syphilology, University of Southern California School of Medicine.

1. University of Chicago Clinics, New York Post-Graduate Medical School and Hospital of Columbia University, State University of Iowa College of Medicine, University of Michigan Medical School, University of California Medical School, Tulane University Graduate School of Medicine, University of Illinois College of Medicine, University of Pennsylvania Graduate School of Medicine, University of Minnesota Graduate School of Medicine, Northwestern University, Massachusetts General Hospital and Mayo Clinic.

The examination of the child revealed the entire tongue and the buccal and the gingival mucous membranes covered with grayish white membranous patches. The vermilion border of the lips was fissured and covered with white scales. A few scaling areas were on the skin of the left cheek. The pharynx and the tonsillar regions were free of exudate. The whitish flakes in the mouth could be easily detached, leaving underlying red hemorrhagic areas. Further examination, including a roentgenogram of the chest, revealed normal conditions.

The urine and the blood were normal. The serologic tests for syphilis were negative. A microscopic examination of the stool showed no Monilia. When cultured on Sabouraud's medium and dextrose agar the stool yielded no fungous

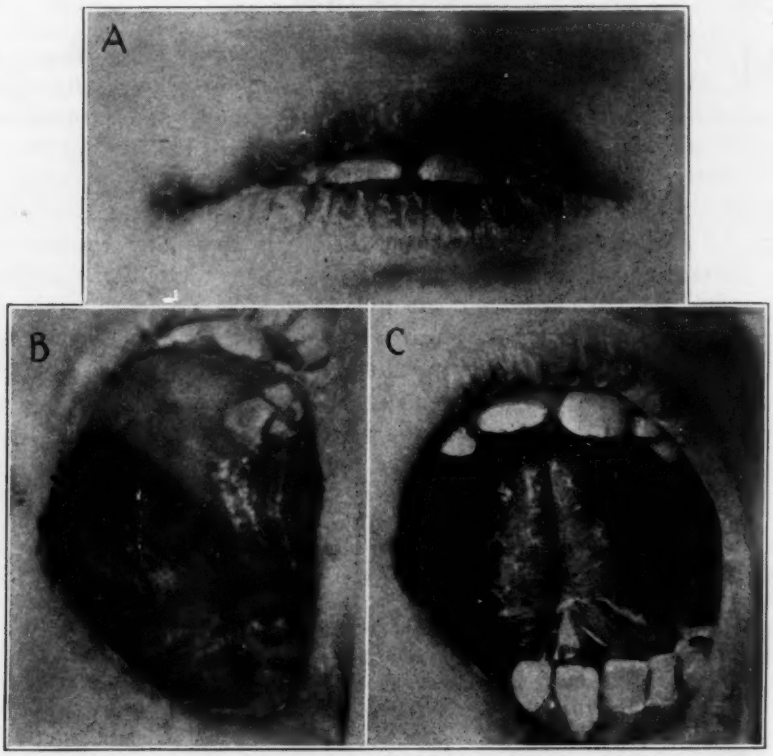

Fig. 1.—*A*, Monilia albicans infection of the lips and the angles of the mouth. *B*, Moniliasis of the buccal and the sublingual mucosae. *C*, Moniliasis of the sublingual mucosa.

growth. Repeated microscopic examinations of direct smears of the exudate of the mouth and the lip revealed various cocci and bacilli and a predominance of Oidium albicans. Repeated cultures of the exudate of the mouth and the lip on Sabouraud's medium yielded a profuse growth of Monilia albicans, recognized on gross and microscopic examination. The clinical and microscopic diagnosis was chronic latent M. albicans infection of mouth, lips and checks.

The child received many types of local treatment for oral thrush, including the application of solution of gentian violet medicinal, Gram's iodine solution, satu-

rated solution of sodium bicarbonate, boric acid solution and 10 per cent neoarsphenamine in glycerin. Strict attention was given to oral hygiene and cleanliness. A diet rich in vitamins was prescribed. Vitamin B complex, nicotinic acid and riboflavin were administered orally in large doses. An autogenous vaccine prepared from the cultural growth was administered subcutaneously in ascending doses three times a week for four months. Gentian violet medicinal and saturated solu-

Fig. 2.—M. albicans cultures on Sabouraud's medium.

tion of potassium iodide were also prescribed orally in large doses in an attempt to correct any possible internal M. albicans infection. None of the local or the internal therapeutic agents prescribed had any effect on the child's disease. The lesions persisted with periods of spontaneous exacerbation and partial remission. Numerous whitish flakes could always be found in the mouth. After four months of poor response of the lesions, all treatment was discontinued.

The girl was not seen again until February 1945. She was now 14 years old and appeared well nourished and in good physical and mental health. Her only complaint was the continued and persistent presence of some white flaky patches

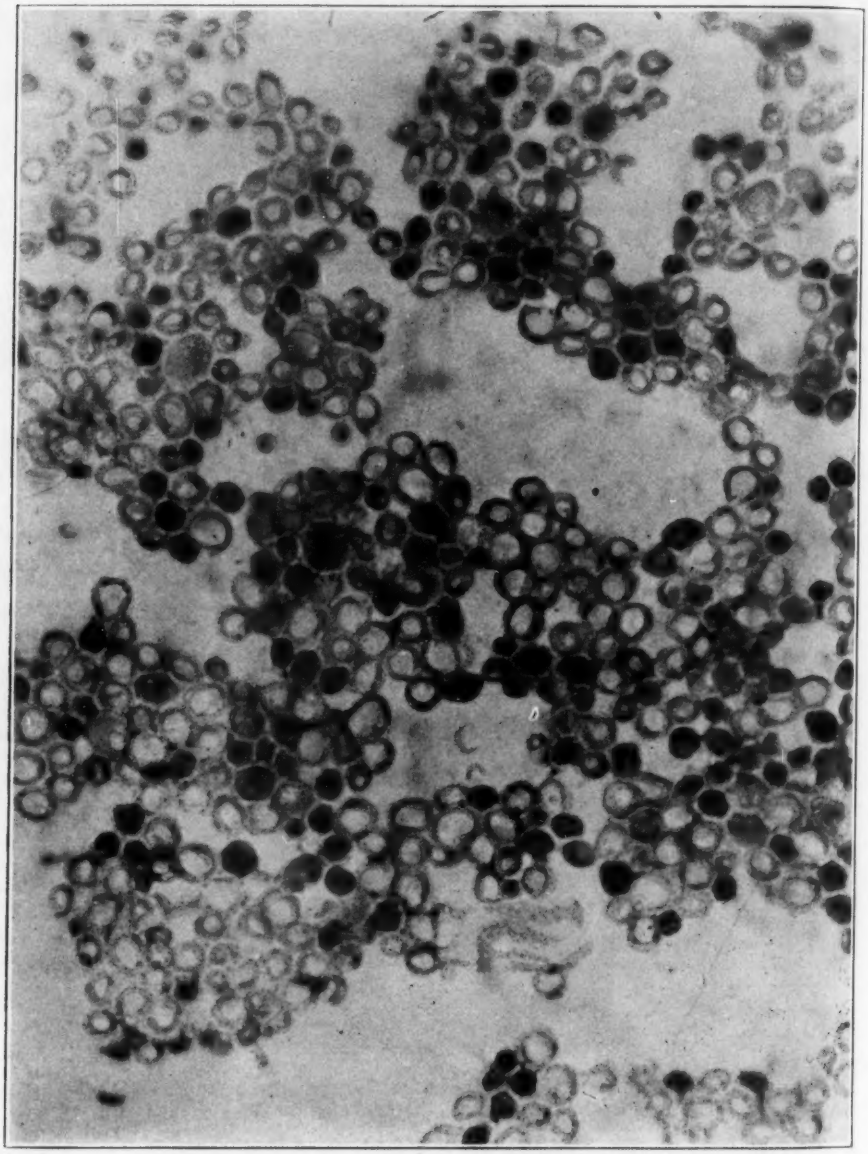

Fig. 3.—Photomicrograph of M. albicans in smear from oral exudate. Methylene blue stain. × 600.

in the mouth. She had practiced strict oral hygiene and cleanliness and daily used a saturated solution of sodium bicarbonate as a mouthwash while away from observation during the seven year interval. Examination revealed a grayish white

exudate on the mucous membrane of the tongue, the cheeks and the lips similar to that of 1938. The lesions, however, were fewer and more superficial as compared with those present at the time of the previous examination. The child was advised to continue using the saturated solution of sodium bicarbonate as a mouthwash.

COMMENT

Castellani [2] has shown that oral thrush may be caused by many species of Monilia and other fungi. Regardless of the type of Monilia responsible for the oral infection, in all cases thrush has been found to present the same clinical appearance. Tobias [3] classifies cases of chronic oral thrush into those of a superficial type and those of a type that is resistant to all known therapy. Our patient's infection belongs to the second type. A critical review of the medical literature reveals few reported instances of chronic latent oral moniliasis of long duration.[4] In the majority of the cases reported, chronic oral thrush has occurred in a marasmic undernourished infant or child. Cachectic adults in the terminal stage of a severe constitutional disease may also have this form of moniliasis. The fungus rarely attacks healthy, well nourished persons. Cases are reported [5] of chronic oral thrush of an apparently harmless type that suddenly became pathogenic and spread to the gastrointestinal tract, the skin, the heart and the lungs. The cause of this change in pathogenicity is unknown. In patients with a less severe type of latent oral moniliasis there may develop diarrheal disease and cutaneous lesions. Our patient's latent oral thrush, however, has persisted for over twelve years, without any apparent harmful effects or evidence of the organism's dissemination.

A survey was made of the incidence and the favored types of treatment of chronic oral moniliasis in large American dermatologic clinics.[1] The results of this survey indicate that the disease presents a timely therapeutic problem. All types of treatment advocated by investigators for chronic oral thrush are reported to yield poor therapeutic response. Figi,[6] from his experience in the department of oral disease at the Mayo clinic, states that chronic thrush of the oral cavity is a process

2. Castellani, A.: Etiology of Thrush, J. Trop. Med. **23**:17 (Jan. 15) 1920.

3. Tobias, N.: Essentials of Dermatology, ed. 2, Philadelphia, J. B. Lippincott Company, 1944, p. 434.

4. Christison, J. T.: A Fatal Case of Thrush Involving the Skin, Lungs and Nails, Am. J. Dis. Child. **26**:250-253 (Sept.) 1923. Schamberg, J. F.: Extensive Fatal Thrush, Arch. Pediat. **32**:617-620 (Aug.) 1915.

5. Schlutz, F. W.: Systemic Thrush in Childhood, J. A. M. A. **105**:650-653 (Aug. 31) 1935. Downing, J. G., and Hazard, J. B.: Cutaneous Moniliasis Associated with Oral Thrush: Unusual Cases, Arch. Dermat. & Syph. **31**:636-643 (May) 1935. Reye, D.: Oesophagitis of Infants, M. J. Australia **2**:673-674 (Dec. 13) 1941. MacGregor, A. R., and Henderson, J. L.: Intestinal Thrush: Report of Two Cases in Young Infants, Arch. Dis. Childhood **18**:186-187 (Dec.) 1943.

6. Figi, F. A.: Personal communication to the authors.

that often persists in spite of all therapeutic measures. There was general agreement among investigators as to the improbability of ultimately curing chronic oral thrush by any known medication, including Oidiomycin desensitization. The survey also revealed the importance that chronic oral thrush may at times assume as a form of precancerosis. Oral leukoplakia and epithelioma superimposed on a chronic thrush infection were reported by Figi in his communication. It is likewise interesting to note that some patients suffering from the disease for years have been reported to show apparent spontaneous cure.

The monilial infection discovered in the mouth and the vagina of our patient's mother indicates the possibility that infants may be infected at birth.[7] As a preventive measure, it would be well for all pregnant women to be examined routinely for vaginal moniliasis. Thorough treatment of those found to have vaginal moniliasis would tend to prevent the fetus from acquiring monilial infection from an infected birth canal.

SUMMARY AND CONCLUSIONS

A survey of dermatologic clinics in the United States indicates that chronic latent oral moniliasis presents an important timely therapeutic problem.

Reports of the development of leukoplakia and epithelioma in chronic latent oral moniliasis in adults indicate that this disease should be classified as precancerosis.

Treatment of vaginal moniliasis should especially be instituted during pregnancy to prevent infection of the fetus as it passes through the birth canal, as suggested in the case reported, in which the mother of a girl with chronic latent oral moniliasis of twelve years' duration had both oral and vaginal infection of the same type.

1930 Wilshire Boulevard.

7. Liston, W. G., and Cruickshank, L. G.: On Thrush, with Special Reference to Vaginal Thrush, Edinburgh M. J. **47**:369-390 (June) 1940. Waters, E. G., and Cartwright, E. W.: Significance of Vulvovaginitis in Pregnancy, J. A. M. A. **113**:30-31 (July 1) 1939. Vayssière, E.: Vulvovaginal Infections Caused by Monilia Albicans, Gynéc. et obst. **24**:644-646 (Nov.) 1931.

EPIDERMOLYSIS BULLOSA

A Recently Described Variant

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SINCE Pels and Goodman [1] described their case of a bullous type of Darier's disease, many similar reports have appeared, but under different titles. "Familial benign chronic pemphigus" was recorded by Hailey and Hailey [2]; Ayres and Anderson [3] called the disease "recurrent herpetiform dermatitis repens"; the term "dyskeratoid dermatosis" was used by Frank and Rein,[4] and Franks and Traub [5] suggested the term "familial benign chronic bullous dermatosis." Many cases are recorded in recent American literature.[6]

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Pels, I. R., and Goodman, M. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier), Arch. Dermat. & Syph. **39**:438 (March) 1939.

2. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **39**:679 (April) 1939.

3. Ayres, S., Jr., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **40**:402 (Sept.) 1939.

4. Frank, S. B., and Rein, C. R.: Dyskeratoid Dermatosis, Arch. Dermat. & Syph. **45**:129 (Jan.) 1942.

5. Franks, A. G., and Traub, E. F.: Familial Benign Chronic Bullous Dermatosis, Arch. Dermat. & Syph. **43**:657 (April) 1941.

6. (*a*) Becker, S. W., and Obermayer, M. E.: Bullous Disease; Bullous Darier's Disease (Pels and Goodman); Familial Benign Pemphigus (Hailey and Hailey); Herpetiform Dermatitis Repens (Ayers and Anderson), Arch. Dermat. & Syph. **41**:1170 (June) 1940. (*b*) Ayres, S., Jr., and Rogers, J. D.: Recurrent Herpetiform Dermatitis Repens, ibid. **42**:490 (Sept.) 1940. (*c*) Halloran, C.: Familial Benign Pemphigus, ibid. **44**:80 (July) 1941. (*d*) Rein, C. R.: Familial Benign Pemphigus (Hailey & Hailey), ibid. **44**:963 (Nov.) 1941. (*e*) Lynch, F. W.: Benign Pemphigus (Hailey and Hailey) Treated with Sulfathiazole, ibid. **43**:736 (April) 1941. (*f*) Goodman, M. H., and Pels, I. R.: Bullous Dyskeratosis of the Keratosis Follicularis (Darier) Type, ibid. **44**:359 (Sept.) 1941. (*g*) Hailey, Howard and Hailey, Hugh: Familial Benign Chronic Pemphigus, South. M. J. **33**:477 (May) 1940. (*h*) Andrews, G. C.: A Case for Diagnosis (Recurrent Dermatitis Herpetiformis Repens?), Arch. Dermat. & Syph. **44**:498 (Sept.) 1941. (*i*) Fraser, J. F.: Chronic Benign Familial Pemphigus, ibid. **46**:592

(Footnote continued on next page)

The aforementioned cases are similar as regards histories, clinical pictures and microscopic data, and most observers agree that they are instances of the same disease. The profusion of names indicates that the exact nature of the disease is not agreed on. This is largely due to different interpretations of the histologic observations. We do not propose to contribute a new legend, but we shall attempt to show that the disease is a variety of epidermolysis bullosa.

Familial benign chronic pemphigus was described by Hailey and Hailey.[2] Obviously, the term "pemphigus" is used only in the histopathologic sense, for clinically there is no resemblance between the disease which they described and pemphigus except for the presence of vesicles or bullae. Three histopathologists who examined sections of the involved tissues made the diagnosis of pemphigus; one examiner thought the sections represented Darier's disease.

The bullous lesion of pemphigus may be intraepidermic; however, it seldom forms just above the basal cell layer and never so uniformly as does the bulla in the Hailey and Hailey disease. Further, the bulla of pemphigus usually contains varying numbers of polymorphonuclear leukocytes, and none is found in the type described by Hailey and Hailey. The vascular changes found in pemphigus, such as swelling of the intima, edema of the vessel wall, perivascular infiltration and congestion of the vessels with blood elements (especially eosinophils), are not present in the Hailey and Hailey disease. These differences indicate that the latter is not related to any type of pemphigus.

The Nikolsky sign may be observed in both diseases and in other bullous diseases. It is therefore by no means pathognomonic of pemphigus. It may be easily explained in the Hailey and Hailey disease by the persistence of lacunas in the lower portion of the epidermis of apparently healed and normal skin which had previously been affected.

Recurrent herpetiform dermatitis repens was described by Ayres and Anderson.[3] The title indicates that this is an exudative inflammatory process in which vesicles or bullae develop, such as are seen in Duhring's disease. These authors admitted that their cases were of the same nature as those of Hailey and Hailey. This disease has the following features: the bullae are intraepidermic; the development is

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(Oct.); (*j*) **46**:326 (Aug.) 1942. (*k*) O'Leary, P. A.; Montgomery, H., and Brunsting, L. A.: Incipient Darier's Disease (?); Benign Pemphigus of Hailey and Hailey (?), ibid. **47**:728 (May) 1943. (*l*) Wise, F.: Dyskeratoid Bullous Dermatosis, ibid. **47**:746 (May) 1943. (*m*) Becker, S. W.: Dyskeratosis Bullosa (So-Called Benign Familial Pemphigus), ibid. **48**:217 (Aug.) 1943. (*n*) Montgomery, R. M.: Familial Benign Chronic Pemphigus, ibid. **50**:53 (July) 1944. (*o*) Ludy, J. B.: A Case for Diagnosis (Dermatitis Herpetiformis? Benign Chronic Pemphigus?), ibid. **49**:362 (May) 1944. (*p*) Ayres, S., Jr.: A Case for Diagnosis (Chronic Benign Pemphigus?), ibid. **49**:458 (June) 1944.

sudden; inflammation is absent or neglible; there are no sequelae, and finally, the incidence is familial. These features are not present in dermatitis herpetiformis; therefore, it does not belong in this group. Siemens [7] refers to cases presented as instances of familial dermatitis herpetiformis which he concluded were really examples of atypical epidermolysis bullosa.

The cases of Frank and Rein [4] were identical with those in the other reports. Although clearcut dyskeratosis was not present, a low power microscopic examination revealed a picture that was vaguely similar to dyskeratosis. For this reason and because it avoided any suggestion of pemphigus, the term "dyskeratoid dermatosis" was advanced. However, the term is unsatisfactory as we shall explain.

Some pertinent features of the pathologic data in the paper by Frank and Rein should be noted. One of us (W. S.) examined all the sections for the authors and found that in tissue taken from skin which had previously been involved small lacunas were present just above the basal cell margin. Such lacunas are not present in similar areas of keratosis follicularis (Darier). Further, the lesions developed rapidly, even in less than an hour. The papillary bodies were intact, with the basal cell margin attached to them. The inflammatory process was negligible, especially in the early stage of the disease. When the process subsided, erythematous patches developed, and the cellular reaction was somewhat more pronounced. Finally, there were some slight, but uncharacteristic, changes in the elastic tissue; occasionally this tissue was missing, and at other times it was fragmented.

Franks and Traub [5] also described this same dermatosis and eliminated all the controversial points by calling it "familial benign chronic bullous dermatosis," which included the main features of the disease. Yet the same term could just as well be used for epidermolysis bullosa.

Pels and Goodman considered this disease a bullous variety of Darier's disease, because they interpreted the microscopic observations as those of true dyskeratosis. We do not believe that it is Darier's disease, either clinically or microscopically.

Clinically, there is little resemblance between the so-called bullous Darier's disease and Darier's keratosis follicularis. While a familial history is found with regard to each disease, Cockayne [8] has pointed out that in Darier's disease "a striking feature is the small number of cases occurring in the family groups, the two with the greatest number

7. Siemens, H. W.: Ueber die Differentialdiagnose der mechanisch bedingten Blasenausschläge, mit Beiträgen zur Kasuistik der sogenannten Epidermolyis bullosa (Bullosis mechanica symptomatica and Bullosis Spontanea congenita) und der hereditären Dermatitis herpetiformis, Arch. f. Dermat. u. Syph. **139**:80, 1922.

8. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, London, Oxford University Press, 1933, p. 137.

containing 7 and 6 respectively." As many as 27 cases of the Hailey and Hailey disease in three generations of a family have been recorded by Becker and Obermayer.[8a] This evidence is striking in view of the long recognition of Darier's disease, in contrast with that of Hailey and Hailey, which was first described in 1939.

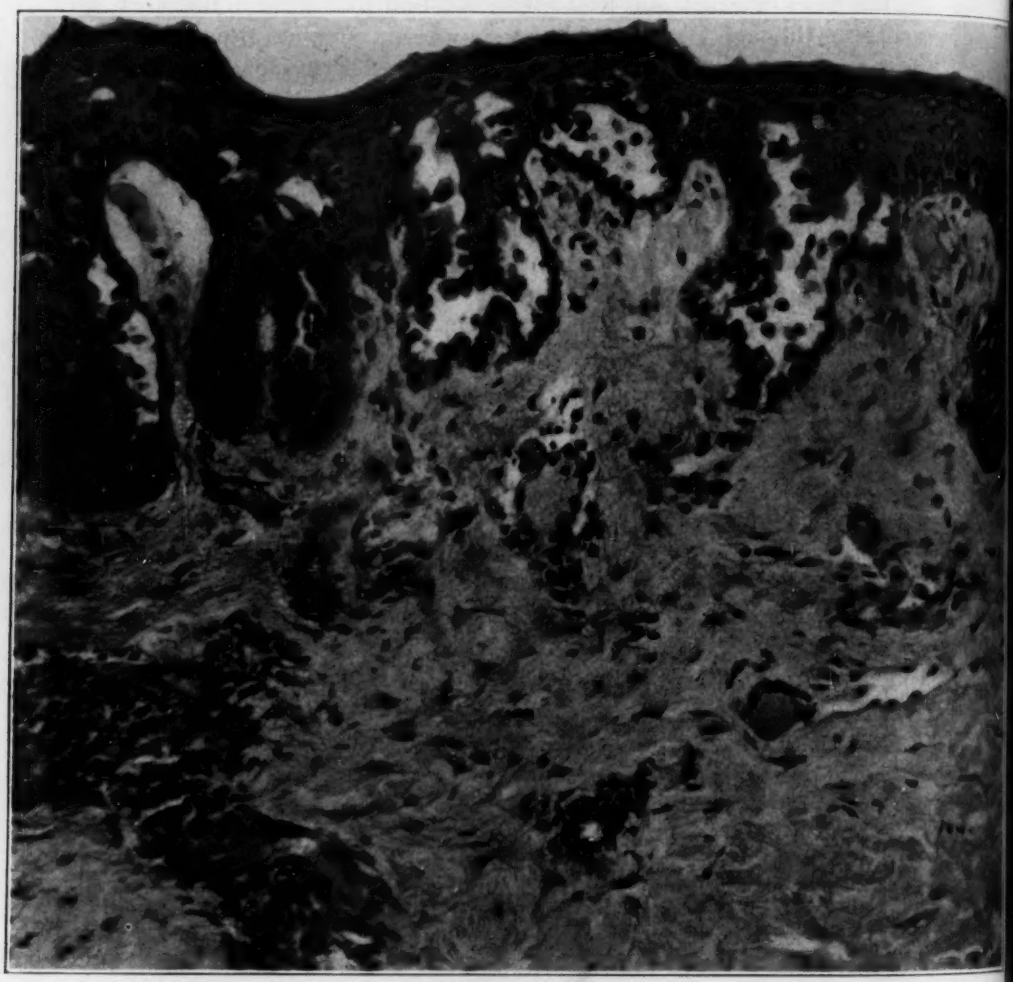

Fig. 1.—Photomicrograph showing the splitting of the epidermis above the basal cell margin, the normal epidermis above the split and a moderate cellular reaction in the cutis; × 260.

In Darier's disease the lesions develop anywhere on the body and are isolated, dull in color and verrucous. In the so-called bullous variety the lesions are chiefly over areas subject to irritation and are not

verrucous and in receding lesions erythematous patches develop, which at times simulate neurodermatitis.

Dyskeratosis is a change in the normal life cycle of the cell or a change in the normal keratinization. This process is inherent in the

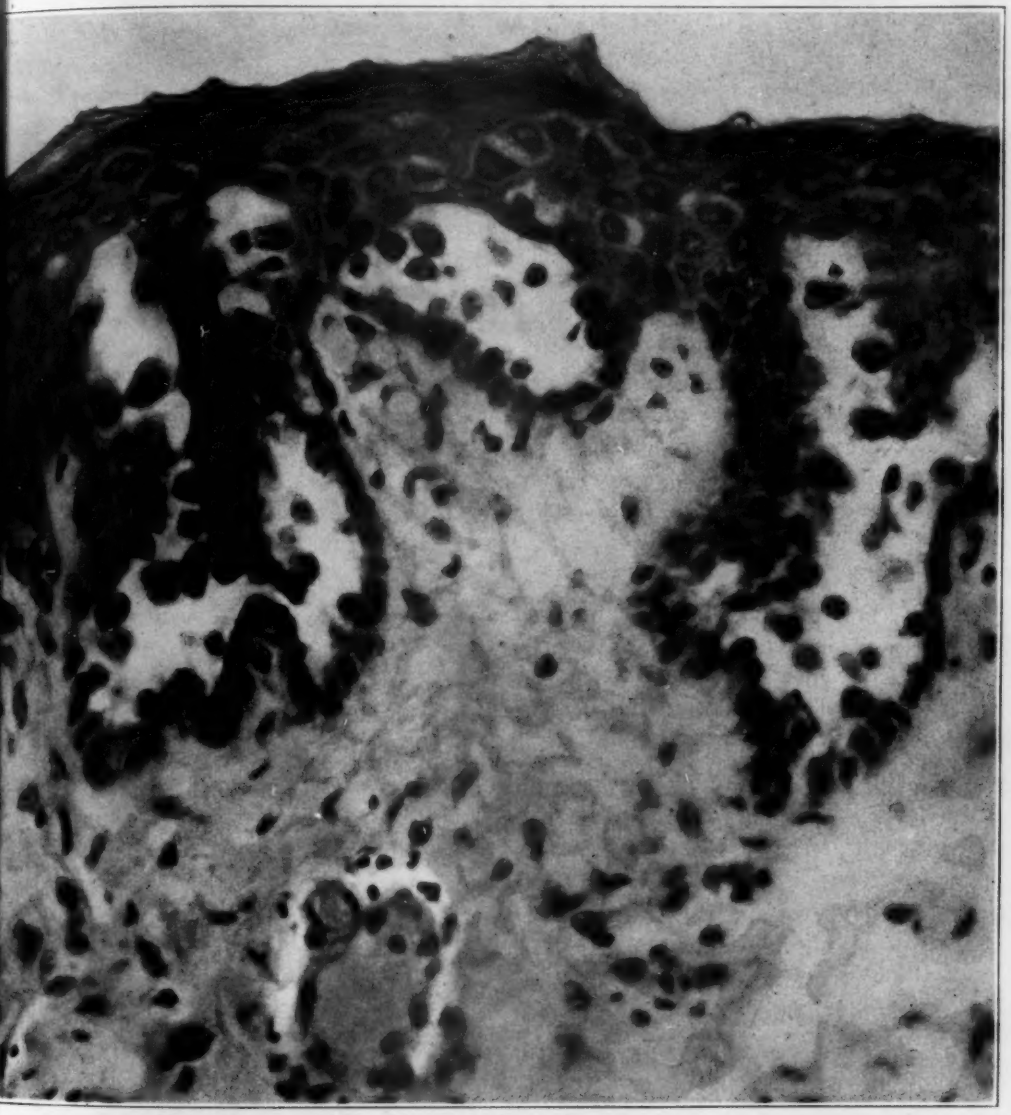

Fig. 2.—Higher magnification of figure 1 showing the normal epidermis above the split and the basal cell margin beneath the split; × 520.

cell and is not part of, or dependent on, inflammation. Thus, hydrops, parenchymatous edema, parakeratosis, ballooning degeneration and

alteration cavitaire are not dyskeratosis. Dyskeratosis either is or is not present, so it is incorrect to speak of a process being dyskeratosis-like or dyskeratoid.

The so-called bullous Darier's disease is not dyskeratosis for the following reasons:

1. The lesions of Darier's keratosis follicularis develop slowly, while those of the so-called bullous Darier's disease form rapidly. This is shown not only by clinical evidence but also by the presence of intact papillary bodies.

2. Darier's disease is accelerated dyskeratosis and as such is an irreversible process. That is, once the cell starts to become hyalinized it cannot return to normal. In the early stage there may be a few hyalinized cells in the lower border of the epidermis with normal cells above them, but after the process has been present for a short time no normal epithelial cells are to be found in the area. Normally, as the cells of the epidermis mature, the basal cell becomes the prickle cell, the prickle cell becomes the granular cell and the granular cell becomes the horn cell. But, once dyskeratosis commences and the lower cells become hyalinized, the cells can no longer become, or change back to, normal prickle cells or granular cells. In the disease described by Pels and Goodman a normal epidermis may be found above the process even in well developed lesions (fig. 1 and 2).

3. Edema is not a component of, nor does it take part in the production of, dyskeratosis. In Darier's disease there is little evidence of edema in the cutis, and whatever tissue fluid was originally present in the epidermis disappears as the cells go on to complete hyalinization. Fluid, is, however, present in considerable amounts in so-called bullous Darier's disease.

4. The presence of an occasional *corps rond* does not justify the classification of this process as dyskeratosis. Darier,[9] who first defined the term "dyskeratosis" in 1900, stated that it should be reserved for those diseases in which this change is predominant and characteristic. The size and the shape of a few cells in some sections from the sites of so-called bullous Darier's disease give them the appearance of being dyskeratotic, but this aspect is neither predominant nor characteristic.

5. In dyskeratosis the cells are smaller than normal, but in the disease described by Pels and Goodman the opposite is true (fig. 3). Here there is acantholysis (i. e., breaking of the intercellular bridges), and the cells separate; they become round rather than polygonal because of surface tension. It is plausible to suppose that such a cell may absorb some of the surrounding fluid, resulting in intracellular or parenchyma-

9. Darier, J.: Précis de dermatologie, ed. 4, Paris, Masson & Cie, 1928, p. 290.

tous edema. The cytoplasm is normal and not hyalinized, as one finds in *corps ronds*. The nuclei are not degenerated but are well formed, well stained, rather large and have distinct nucleoli. Mitotic figures are

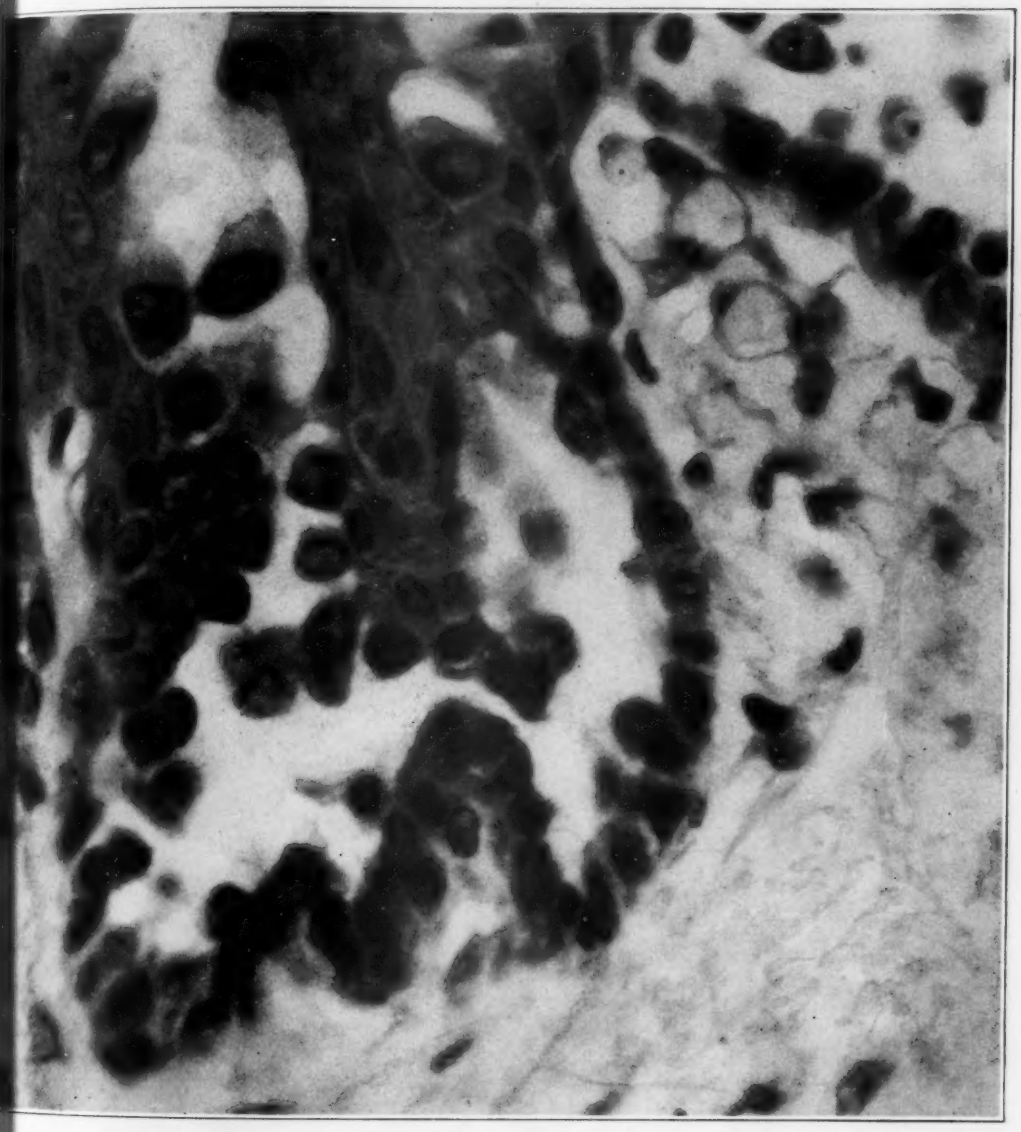

Fig. 3.—Higher magnification of figure 2 showing enlarged round epithelial cells with distinct, well stained nuclei; × 1700.

frequently seen in the disease under discussion, but they are never part of accelerated dyskeratosis (fig. 4).

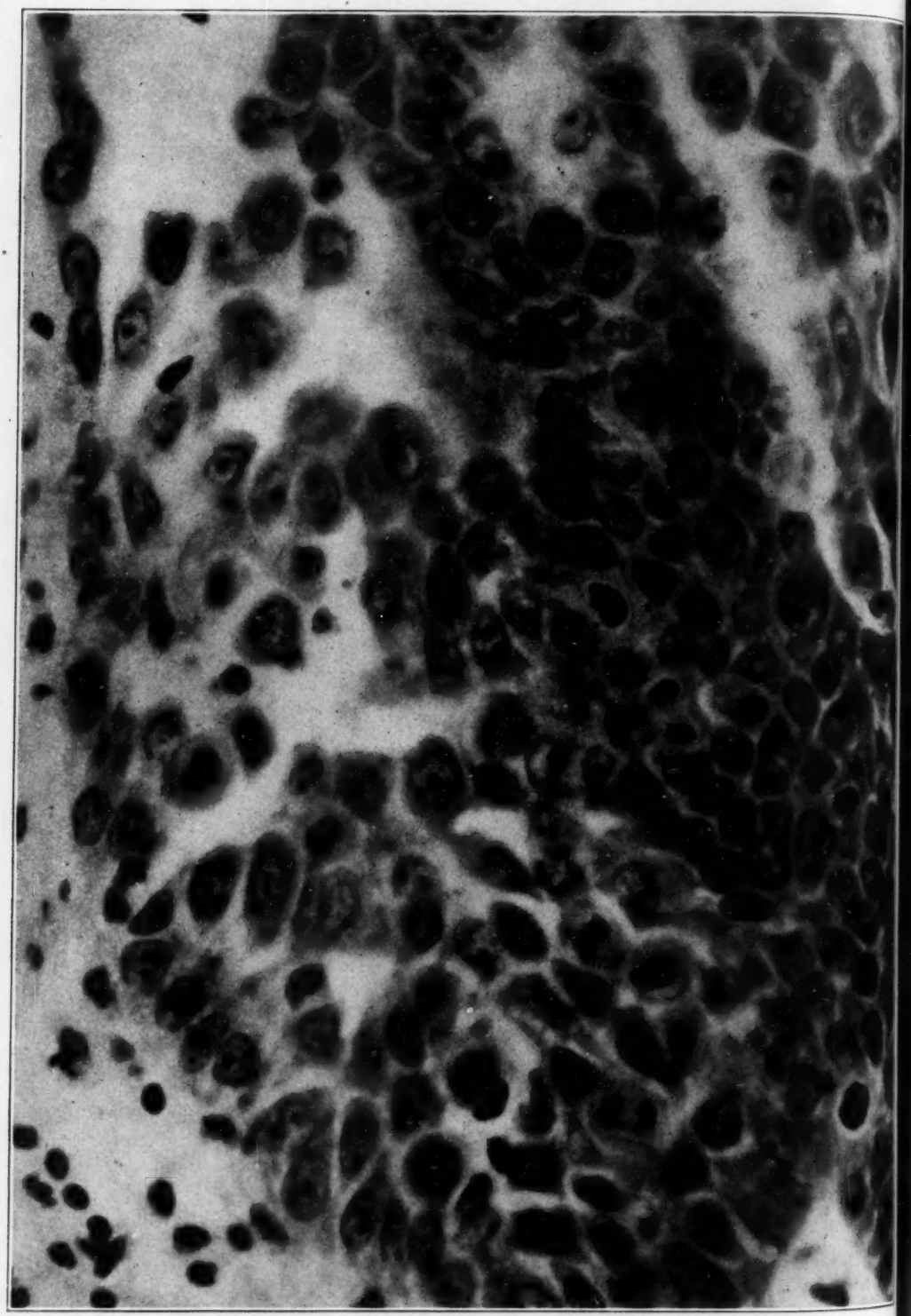

Fig. 4.—High power photomicrograph of a lesion showing acantholysis, large round epithelial cells with large, well formed and stained nuclei and many mitotic figures; × 1700.

6. In keratosis follicularis there is no parakeratosis; an increased horny layer dips into the epidermis, and the process, beginning in the basal cell layer itself, may occur in small focal areas. In this disease, however, parakeratosis is present; the horny layer is not increased, and the process, beginning above the basal cell margin, may extend over large areas.

7. As mentioned before, in sections of skin examined for Frank and Rein lacunas were found just above the basal cell margin of tissue taken from clinically normal skin which had previously been affected. To our knowledge this has not been described as a characteristic of Darier's disease. We believe that the lacuna found in Darier's disease is not due to edema but is probably of mechanical origin. The cells in the affected area are dyskeratotic and form *corps ronds,* which, occupying less space than normal prickle cells, cause the epidermis to split.

To summarize, the features not found in dyskeratosis are: the rapidity of the development of the process, as indicated by intact papillary bodies; the normal epidermis above a well established lesion; the presence of edema; the size, the shape and the staining properties of the cell body and the nucleus; the activity of the cells, as indicated by the presence of many mitotic figures; the frequent presence of parakeratosis, and the persistence of lacunas in the lower portion of the epidermis after the clinical disappearance of the lesion.

The relationship of bullous Darier's disease to epidermolysis remains to be discussed. The following histologic features coincide with those of epidermolysis bullosa: the absence of dyskeratosis, the suddenness of the process, the bullous lesion, the unaltered papillary bodies, the lack of inflammatory cells in the bulla and the changes of the elastic tissue.

The intraepidermic site of the lesion is entirely comparable with that of the simple, dominantly inherited, nondystrophic epidermolysis bullosa. It is only necessary for one to recall the earlier nomenclature to conclude that epidermolysis bullosa was considered an epidermic process and given such names as "acantholysis bullosa" (Goldscheider and Joseph [10]) and "congenital traumatic pemphigus" (Crocker [11]). Accordingly, there is no reason for using any of the different names suggested recently for the disease under discussion. "Acantholysis bullosa" or "epidermolysis bullosa" is correct from the histologic point of view.

The high familial incidence found in regard to this disease is also found in regard to epidermolysis bullosa.

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10. Goldscheider, A.: Hereditäre Neigung zur Blasenbildung, Monatsh. f. prakt. Dermat. **1**:163, 1882.

11. Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 293.

Classic epidermolysis bullosa occurs on exposed areas and over the joints which are sites of predilection for trauma; in this disease the favored areas are the intertriginous and the unexposed parts. It is this difference that has probably prevented most observers from correlating the two diseases. However, epidermolysis bullosa has been described as appearing in other than the classic areas (e. g., about the neck, from the rubbing of a collar). The site of the disease, moreover, should not, in the face of overwhelming evidence to the contrary, prevent one from putting this disease into the epidermolysis bullosa group.

SUMMARY

Evidence is submitted to show that the disease variously described as familial benign chronic pemphigus, recurrent herpetiform dermatitis repens, dyskeratoid dermatosis, familial benign chronic bullous dermatosis and bullous Darier's disease is not pemphigus, dermatitis herpetiformis or Darier's disease.

We have attempted to prove that this disease is a form of epidermolysis bullosa.

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BENADRYL IN DERMATOLOGIC THERAPY

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THOUGH there remains doubt as to the mechanism of production of the urticarial wheal and other reactions of allergy, most of the recent work has been based on assumption that such reactions are mediated by histamine or an H substance. Attempts at therapeutic desensitization toward histamine have utilized histamine as well as a conjugated hapten, but this approach has been time consuming and not uniformly successful. Because of its antihistamine effect Curtis and Owens [1] recently called attention to betadimethylaminoethyl benzhydryl ether hydrochloride (Benadryl),[2] which they used in the treatment of acute and chronic urticaria. The drug is many times more effective than theophylline ethylenediamine in alleviating histamine shock and anaphylactic shock in the guinea pig.[3] It appears to reduce bronchoconstriction, abolish vasodepressor effects and exert an antispasmodic action. Toxic effects are few and were reviewed by Curtis and Owens in their report on treatment of 18 patients with various types of urticarial eruptions. Eleven patients had almost complete relief, and 3 more had considerable relief, while 4 did not respond to the treatment. Two patients complained of drowsiness and muscular aching, and 1 had to stop treatment because of weakness and vertigo. The authors pointed out that the effectiveness was only palliative but that no cumulative toxic effects were noted in patients who continued to take the drug for as long as seven months.

From the Division of Dermatology, University of Minnesota, Dr. H. E. Michelson, Director.

1. Curtis, A. C., and Owens, B. B.: Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Treatment of Acute and Chronic Urticaria, Univ. Hosp. Bull., Ann Arbor **11**:25 (April) 1945.

2. The name "Benadryl" has been applied by Parke, Davis and Company to the following drug: beta dimethylaminoethyl benzhydryl ether hydrochloride. For this study generous supplies of the drug were made available by Mr. Paul S. Denn of the Medical Service and Dr. E. A. Sharp of the Department of Clinical Investigation of Parke, Davis and Company.

3. Loew, E. R.; Kaiser, M. E., and Moore, V.: Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, J. Pharmacol. & Exper. Therap. **83**:120 (Feb.) 1945. Loew, E. R., and Kaiser, M. E.: Alleviation of Anaphylactic Shock in Guinea Pigs with Synthetic Benzhydryl Alkamine Ethers, Proc. Soc. Exper. Biol. & Med. **58**:235 (March) 1945.

The present report deals with the administration of Benadryl to 90 patients, of whom 33 had urticaria and the remainder had a variety of dermatologic manifestations. In most instances the drug was given orally with initial dosage of 50 mg. six times daily, though a few patients received only four doses and others as many as eight doses in the first twenty-four hours. The drug was given intramuscularly in 1 case and intravenously in a dosage of 10 to 20 mg. in several instances, in addition to oral administration. Single doses for children were 25 mg. orally or 5 mg. by vein. In no case did the dosage exceed 400 mg. per day, and in all instances the dosage was reduced as rapidly as relief was obtained, usually remaining at 50 to 150 mg. daily for a prolonged period if the urticaria had been present for any considerable time. In the cases of more acute disease it was soon possible to stop the use of the drug.

ACUTE URTICARIA

In 4 of 10 cases of acute urticaria (present from six hours to fourteen days) there was striking relief within twenty-four hours; in 5 more instances there was complete recovery but at a rate such as

Results of Benadryl Therapy

	Number	Complete Relief, Percentage	Moderate Relief,* Percentage	Improved–Indeterminate,† Percentage	Failures, Percentage
Urticaria					
Acute	10	40	..	50	10
Chronic	23	61	26	4	9
Drugs	3	67	33	..	..
Pruritus vulvae	5	60	..	20	20
Insect bites	11	36	18	18	27
Erythema multiforme	4	25	..	50	25

* In these cases relief varied from 50 to 90 per cent.

† These results are regarded as indeterminate because of delayed response or use of additional therapeutic agents.

to leave in doubt the share played by the drug. For example, in 2 instances in which the disease had existed for seven days the patients were not relieved until after four and seven days respectively. Even after intravenous therapy improvement was incomplete at three days in 1 case in which the eruption had been present for ten days before treatment was started. Combined oral and intravenous administration of the drug failed to relieve 1 patient whose eruption had existed for four days; psychic factors appeared to be important in this case. Unfavorable reactions to the drug were few, probably because of the short period of use in acute urticaria. The results of therapy are always difficult to evaluate in an illness the natural course of which is so variable. The failures may have been due to inadequacy of the drug or of the present schedule of dosage; it is a question whether these

eruptions might have responded to larger or more prolonged dosage. Early cessation of treatment was due chiefly to lack of confidence and lack of knowledge.

With use of Benadryl relief can apparently be expected in 90 per cent of cases of acute urticaria, but many of the patients might have experienced similar relief with rest, simple topical applications, sedation or even without treatment. In one instance there was visible relief (i. e., regression of the wheal to simple erythema) ten minutes after intravenous administration of 10 mg. of Benadryl. In several instances the visible and sensory relief was evident in about thirty minutes. One can be reasonably certain that Benadryl has been effective in some cases of acute urticaria. It must be remembered that the title "acute" urticaria is misleading because without effective treatment in some undetermined proportion of the cases the disease would have become more chronic.

CHRONIC URTICARIA

For purposes of review the 23 patients with chronic urticaria were divided into two groups: first, those with the eruption present for one to seven months before Benadryl therapy, and, second, those whose eruptions had persisted one year or more. In the former series were 10 patients, 8 of whom obtained complete relief following treatment. In one instance the results were regarded as indeterminate because relief was incomplete, though probably because of lack of cooperation from the patient, and in another case urticaria which had persisted for seven months was 75 per cent relieved after four weeks of treatment (yet the drug was of considerable value since the eruption again became severe when administration was stopped and improved a second time on reinstitution of therapy). Of the 8 patients with good results several obtained their complete relief within the first forty-eight hours, though usually several days to a week were required. In this group of 10 patients 6 had some discomfort resulting from the drug; dryness of the mouth was noted by 3 patients, lethargy by 2, and vertigo by 2.

The 13 patients in the second group, with urticaria for a year or more, provide even more dramatic evidence of therapeutic efficacy because of the long duration of the disease and its failure to respond to numerous previous therapeutic attempts, contrasted with the rapidity with which improvement was noted and the high incidence and uniformity of satisfactory results. There were 2 cases which were regarded as failures after two weeks of treatment though even in 1 of them there was some improvement. Eleven patients obtained satisfactory relief, from 75 to 90 per cent in 4 instances and complete relief in 7 instances. Relief was regarded as complete in several instances even though one or several hives occurred at intervals of several days or weeks, or visible

but asymptomatic erythema was noted occasionally. In a case of one year's duration complete relief resulted from two hours of treatment, but 1 patient was not fully relieved until five months of treatment for urticaria of three years' duration had been completed. Of the 4 patients with partial relief 2 obtained maximum benefit (80 and 90 per cent) by one week, and others improved steadily to 75 per cent and 90 per cent relief at four weeks.

Of the 23 patients with chronic urticaria there were only 2 who did not have considerable improvement; 1 failed to give complete cooperation; 5 were 75 to 90 per cent relieved and 15 were almost completely relieved of symptoms, though in 1 case the improvement was so slow as to be of doubtful significance. Therapeutic efficacy rather than coincidental improvement is suggested by the fact that 9 had recurrence of the eruption when treatment was stopped and renewed relief after further therapy.

In certain instances of chronic urticaria the rate of improvement was striking: relief two hours after treatment was begun in a case of one year's duration and relief after one day of treatment of a patient whose eruption had been present several years. A different measure of efficiency was the continuously favorable progress in other cases of long duration—for example, steady improvement until complete relief of a patient whose trouble had persisted for ten years.

The case of longest duration was that of a woman 54 years of age who had had urticaria almost daily since childhood. At first she did not tolerate the drug well, complaining of nausea and oral dryness, and she was unwilling to continue treatment though she was 50 per cent improved after two weeks. After further therapeutic attempts by other physicians she returned and offered to submit again to treatment; this time the dosage was smaller at first and was then gradually increased to 200 mg. daily without discomfort and with 90 per cent relief of the urticaria after one month.

URTICARIA FROM DRUGS

Benadryl was given to 3 patients whose severe generalized urticaria followed administration of a drug. In a case in which the eruption had persisted for two days after sulfonamide therapy was stopped there was practically complete absence of itching thirty-five minutes after 50 mg. of Benadryl was given, and the eruption promptly disappeared. In a second case urticaria and severe dermographism had persisted for three weeks after the last dose of sulfonamide compounds and had not responded to repeated injections of histamine in the hospital; this patient was 65 per cent improved after twenty-four hours of Benadryl therapy and was completely relieved at forty-eight hours. The third patient

had a severe eruption of two days' duration with high fever as a result of sensitivity to a barbiturate; though there had been no relief with hospital care the eruption improved in appearance and itching was greatly relieved almost immediately after the first capsule of Benadryl was taken, but the fever persisted several days and pyogenic cutaneous complications developed.

PRURITUS

While some cases of pruritus seem closely allied with atopy and urticaria others appear to be dependent on unrelated factors. Nevertheless, 9 patients were treated with Benadryl, 5 of whom had pruritus vulvae and 4 other types of pruritus. Of the latter group all improved; in 2 the value of the drug could not be estimated, and in 1 the neurotic factor was so large as to leave the result in doubt. The last patient was a woman with generalized pruritus associated with neurotic excoriations and secondary dermatitis of two months' duration; she was 90 per cent improved after two weeks of treatment though a previous attack of the disease had been extremely chronic and had resisted all care but that of a psychiatrist. The fourth patient was an elderly man with generalized pruritus which became 60 per cent better at two weeks and gradually improved to complete relief at ten weeks, followed by recurrence when treatment was stopped and relief later with 150 mg. daily.

Five patients had vulvar pruritus. One also had urticaria (and is included in that review as well); the vulvar pruritus was of more than one year's duration but was greatly improved at the end of one week and completely so in four weeks. A patient with anal and vulvar pruritus for five years was greatly relieved at one week and completely so at three weeks. In 2 instances vulvar pruritus of one month's duration was then complicated by generalized pruritus; in 1 case the patient experienced "immediate" relief of the generalized symptoms, but the vulvar eruption required further care, and in the other the patient was much better after two days of treatment and was cured after ten days. There was complete failure in 1 case, in which vulvar pruritus had been present for one month.

INSECT BITES

Because of the urticarial nature of the cutaneous reaction to insect bites Benadryl was given to 11 patients suffering from various types of bites. There was apparent failure to respond in 3 cases, in 2 of which there were tense swollen reactions to the sting of a bee. In 2 instances the response was favorable but slow, and the value of the drug could not be judged. The remaining patients had more chronic, severe and extensive urticarial papules after frequently repeated bites from fleas, bedbugs or mosquitoes. With continued exposure to the insects there was improvement varying from 50 per cent (in 2 instances) to complete

relief in two days (1 case) to relief within the first several hours (3 cases). Several additional cases were not included in the review because of complete inability to judge the value of the drug.

VARIA

In three apparently unrelated diseases there were experiences which suggest the advisability of further and more prolonged therapeutic trial with Benadryl. There was slow but steady improvement in the case of 2 patients with the papular form of rosacea. Although Benadryl was given concurrently with other therapy, the latter had previously been administered to these patients with little or no favorable effect.

Benadryl was tried in 4 cases of erythema multiforme because of the statement of Curtis and Owens that it appeared to be of value. In 1 instance the eruption followed a rather mild course, but the patient had on a previous occasion suffered a mild course, though more frequently the course had been more severe. Another patient was completely relieved at one week, a somewhat indeterminate event. The third case was that of a woman with an extensive nodular eruption, resembling erythema nodosum, but with the distribution characteristic of erythema multiforme. Two previous attacks had been so severe as to require hospitalization for five and ten days respectively. The current attack began with equal severity and acuity, but the eruption was greatly improved twenty-four hours after 20 mg. of Benadryl had been given intravenously and 50 mg. every four hours. This treatment was continued; at three days the eruption had disappeared except for bluish red discoloration at the sites of former nodules, and a few days later there remained no visible trace of inflammation. At no time was the patient toxic. In the fourth case a rather severe papular eruption responded in four days with disappearance of all but the erythema; the results were judged to be indeterminate as to the part played by the drug.

Benadryl was given to only 1 patient with lupus erythematosus. A previously chronic facial eruption had nearly disappeared after treatment of her bronchitis and chronic sinusitis by local, oral and surgical measures. Acute recrudescence of the eruption was associated with exacerbation of the sinusitis because of allergic rhinitis. The cutaneous lesions were bright red and urticarial in nature, and were present on the cheeks and the upper surface of the chest. After Benadryl was administered in doses of 300 mg. daily for six days the nasal condition and the eruption were greatly improved. The lesions disappeared from the chest and the facial lesions became much less acute in appearance. Was the action directly on the eruption or indirectly by way of the improvement in the sinusitis following relief of the rhinitis?

FAILURES

There was apparent lack of success with 6 patients with neurodermatitis, 2 with contact dermatitis, 2 with dermatitis unclassified as to type, 2 with dermatitis herpetiformis and 1 with periarteritis nodosa. Aphthous stomatitis failed to respond in 1 instance, but in a case in which glossodynia and stomatitis were accompanied by urticaria all symptoms responded well to treatment. Numerous other patients were treated but not included in the report because of inadequate information.

SUMMARY

During the past six months Benadryl has been administered to about 90 patients with diseases of the skin. It has not been possible to draw conclusions from every case: Some patients failed to return or to provide sufficient information; others improved but had diseases which usually disappear without treatment or were given additional therapeutic measures, but the majority of the patients were untreated by other methods, had chronic illnesses or had treatment withdrawn and reinstituted in such a manner that the results can be regarded as conclusive.

Of 33 patients with urticaria, all but 3 obtained satisfactory relief. It may be of note that all 3 patients treatment of whom failed showed strong psychoneurotic tendencies. In 6 further instances the rate of improvement was such as to cast some doubt on the therapeutic effectiveness; perhaps this conclusion is too conservative to be fair and possibly those patients and the frank failures would have benefited from more intensive or prolonged therapy. In 24 cases, 73 per cent, the improvement or cure can probably be credited to Benadryl.

Approximately 30 per cent of the patients with urticaria had discomfort from taking the drug (oral dryness, lethargy, vertigo, nausea or slight agitation and apprehension), but in no instance was the reaction severe and all but 1 patient were anxious to continue taking the drug. There was limited experience with intravenous administration, but several patients felt weak and faint after 10 to 20 mg. had been given in that manner. Such reactions were transitory, and in 1 case there was notable improvement of the eruption during and after the short period of reaction. Therapeutic effectiveness without objectionable reaction seems unquestioned in urticaria, particularly in its more chronic forms. In many instances (at least 50 per cent) of chronic urticaria the relief is dependent on continued regular administration of the drug in doses of 50 to 150 mg. daily, but there has been no noticeable evidence of cumulative toxicity from such prolonged dosage.

Benadryl appears to be particularly efficacious in treatment of urticarial hypersensitivity to drugs; the relief was obtained rapidly in 3 such cases.

Based on experience in 11 cases of insect bites Benadryl appears to be effective in about 60 per cent of the cases. Further experience will be needed to determine whether the failures can be explained on individual differences, the nature of the insect, inadequate dosage, etc.

With limited experience in treating pruritus it seems that Benadryl is helpful in 60 per cent of cases of vulvar pruritus. It deserves much more extensive trial in all forms of local and general pruritus.

Results have been inconclusive but somewhat encouraging in erythema multiforme, rosacea and perhaps lupus erythematosus. There was failure in various forms of eczema and in dermatitis herpetiformis.

From these results of therapeutic trial in various dermatoses it may be concluded that Benadryl is a useful and welcome additional aid the therapeutic possibilities of which have not yet been thoroughly studied but which has undoubted value in dermatotherapy.

Clinical Notes

VON RECKLINGHAUSEN'S DISEASE

Traced Through Five Generations

LAWRENCE FRANK, M.D., BROOKLYN

The familial incidence of multiple neurofibromatosis, or von Recklinghausen's disease, has long been noted, and most authors today accept the fact that there is a hereditary transmission of the disease. Harbitz,[1] in a review of multiple neurofibromatosis, reported a case of elephantiasis of the left lower extremity and stated that a similar condition had existed in four previous generations. He termed the disease "elephantiasis neuromatosa congenita." Castellino[2] stated, "The disease assumes a familial character and may be transmitted to the first, second or third generations." Preiser and Davenport,[3] in a review of cases in which there were two or more offspring of an affected parent, found that of 115 offspring 50 were affected and concluded, as did Cockayne,[4] that the defect is a simple dominant.

The following is a report of a case in which von Recklinghausen's disease can be traced through five generations. The patient, 4 of the patient's 5 children and the patient's grandchild, all have been found, on examination, to have the disease. The patient stated that both her mother and grandmother were similarly affected.

REPORT OF A CASE

M. R., a 72 year old white woman of German descent, was admitted to the hospital on Jan. 8, 1946 because of ulceration and hemorrhage of a tumor mass on her right thigh. The ulceration occurred after a fall two weeks prior to her admission.

A physical examination revealed several hundred tumors covering the patient's body. The tumors varied in size from a small pea to a hen's egg. No single area of the body was free of lesions. Some of the growths were small nodules in the subcutaneous tissue. Some were soft, fleshy or rubbery. Many were firmer and almost gave the impression of being mamillated. On the right thigh one of the larger tumors was ulcerated; the epidermis was retracted, and a granular bleeding surface was exposed. This was the only lesion tender to pressure. Two other tumors on the same leg were reddish blue and suggestive of internal hemorrhage. The remainder were flesh colored or hyperpigmented. There were multiple hyperpigmented patches present on the patient's body varying in size from that of a dime to that of a saucer.

From the Skin and Cancer Hospital, Philadelphia.

1. Harbitz, F.: Multiple Neurofibromatosis: Von Recklinghausen's Disease, Arch. Int. Med. **3**:32 (Jan.) 1909.

2. Castellino, P. G.: Familial Recklinghausen's Disease: Clinical and Pathological Contribution, Urol. & Cutan. Rev. **34**:384 (June) 1930.

3. Preiser, S. A., and Davenport, C. B.: Multiple Neurofibromatosis and Its Inheritance, Am. J. M. Sc. **156**:507 (Oct.) 1918.

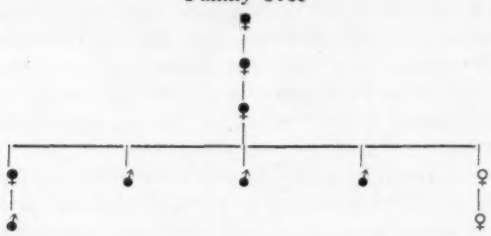
4. Cockayne, E. A.: Inherited Abnormalities of the Skin, London, Oxford University Press, 1933.

The patient stated that these nodules had first appeared at the age of 12 years and had continued to appear for the past sixty years. She was diabetic and had been taking insulin until six years previously. Her blood sugar level was found to be 265 mg. per hundred cubic centimeters.

Four of the tumors, including the ulcerated one, were removed. On section one of the tumors was found to contain a large blood clot. A histologic study revealed neurofibroma.

The patient's 3 sons, 2 daughters and 2 grandchildren were examined. The 3 sons, 1 daughter and her child (patient's grandchild, 19 years of age) were found to be affected with numerous sessile and pedunculated tumors. Patches of hyperpigmentation were also in evidence. Examinations of the other daughter and her child (patient's grandchild, 14 years of age) showed no lesions or pigmentation suggestive of von Recklinghausens disease.

Family Tree



♀ ♂ Von Recklinghausen's disease present
♀ No indication of von Recklinghausen's disease

COMMENT

It is of interest to note that the mother was diabetic in view of the fact that many believe that an endocrine dyscrasia is frequently present in patients with this disease. Further, the 3 sons, although over 25 years of age, were not married. With the disease an inherited dominant, nature finds other limitations by natural selection.

SUMMARY

A family is presented in which von Recklinghausen's disease can be traced through five generations. The disease was found in three generations by personal examination and in two through the history reported by the patient.

573 Sixteenth Street.

DERMATITIS FROM CONTACT WITH VARNISH OF JAPANESE RIFLES

LIEUTENANT COMMANDER RALPH B. COOMBER, MC-V(S), U.S.N.R.

During the occupation of Japan, many thousands of confiscated Japanese rifles were issued as souvenirs to the members of the occupying forces. Soon thereafter a striking increase was noted in the percentage of cases of contact dermatitis referred to the U. S. S. Benevolence, then serving in the Tokyo Bay area. In many of the cases in which a contact factor was suspected, questioning revealed

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a history of the patient's having handled a Japanese rifle a day or two prior to the onset of the cutaneous manifestation. These cases usually presented the picture of an acute erythema accompanied with varying degrees of edema and in some cases vesiculation. The regions involved were usually the hands and forearms and, in some cases, the inner surfaces of the legs and ankles. The dermatitis involving the latter areas was explained by the fact that the rifle stock was often held between the legs while the rifle was being examined or worked on. In cases in which the varnish had been scraped an accumulation of varnish particles in the socks was suspected of having caused the dermatitis of the ankles. Under treatment with wet dressings, calamine lotion or solution of calcium hydroxide, the eruption cleared promptly, and, with avoidance of further contact with the rifles, no recurrences were encountered.

REPORT OF A CASE

Lieutenant Commander J. L. E. noticed redness and burning on the flexor surface of each forearm. The previous afternoon he had undertaken to remove, with sandpaper, the finish from the stock of a Japanese rifle. No other unusual contacts could be elicited in the history. Examination revealed an acute erythematous dermatitis of the flexor surface of each forearm, with a number of minute elevated papules present. A similar type of erythema was present on the dorsum of each hand and on the lateral surfaces of the fingers, but with less edema. There was no involvement of the skin of the other surfaces of the body. With a razor blade, a small amount of varnish was scraped from the stocks of several Japanese rifles. This in turn was mixed with acetone, following which some of the solution was applied to the flexor surface of the patient's arm and covered with wax paper. A similar test, using acetone only, was applied to the opposite arm, as a control. At the end of twenty-four hours the patient noticed considerable itching at the site of the patch which contained the varnish, and at the end of forty-eight hours removal of the patch disclosed a sharply demarcated, elevated erythematous area. The patch test with acetone elicited a negative reaction.

Inasmuch as many thousands of Japanese rifles will have been brought back to the United States by returning servicemen, it is conceivable that instances of contact dermatitis will develop from the handling of these weapons. It is suggested that this be borne in mind when one is searching for etiologic factors in contact dermatitis.

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MYCOSIS FUNGOIDES AND SIMILAR CONDITIONS IN THE NEGRO

H. H. HAZEN, M.D., WASHINGTON, D. C.

A recent article by Sigel [1] calls attention to the tradition that mycosis fungoides is much less frequent in the Negro than in the white person and quotes a number of other dermatologists, mostly from the West, to the same effect. A brief survey of modern textbooks on dermatology shows that their authors express the same opinion. In 1911 Strobel and Hazen [2] expressed the same

1. Sigel, H.: Mycosis Fungoides in the Negro, Arch. Dermat. & Syph. **52:** 18 (July) 1945.

2. Strobel, E. R., and Hazen, H. H.: Mycosis Fungoides in the Negro, J. Cutan. Dis. **29:**147, 1911.

opinion in reporting a case. They quoted Bloodgood as having seen 1 previous case. In 1914 Bernard Wolff [3] reported another example.

Only one author has reported a long series of personally observed consecutive cases of cutaneous diseases in the Negro.[4] He reported observations on 11,729 consecutive cases of cutaneous diseases, excluding syphilis, in the Negro in Washington, D. C.; 9 cases of mycosis fungoides were found. The opinion was then expressed that the disease was less frequent than in the white race.

Up to the present time a total of 14,100 consecutive cases of diseases of the skin, again excluding syphilis, have been seen by me. In this series there were 14 cases of mycosis fungoides, a percentage of 0.1.

Regarding the frequency of the disease in the white race, figures vary from 0.03 per cent, of Pollitzer,[5] to 0.24 per cent, of Crocker,[6] in private patients. It is interesting to note that Sigel, in a small series of cases, found nearly equal frequency in the two races.

It is generally agreed that mycosis fungoides is much more frequent in the Negro woman than in the Negro man, while Crocker reported a higher frequency in the white man than in the white woman. According to all authors the clinical features are the same in the two races.

Kaposi's sarcoma is apparently rare in the Negro; I have seen but 2 patients, both men.

Cutaneous lesions of leukemia are also rare in the Negro race; 3 instances have been seen, a case of acute splenomyelogenous leukemia in a young child, who presented multiple nodules over the body.

Two instances of Hodgkin's disease with cutaneous conditions were observed.

CONCLUSIONS

Mycosis fungoides is somewhat less frequent in the Negro race than in the white race, but it is not nearly so uncommon as has been stated. Kaposi's sarcoma, leukemia cutis and the cutaneous lesions of Hodgkin's disease are so rare in the Negro that it is impossible to compare the relative frequency of these diseases in the two races.

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3. Wolff, B.: Mycosis Fungoides Occurring in a Negress, J. Cutan. Dis. **32**:440, 1914.

4. Hazen, H. H.: Syphilis and Skin Diseases in the American Negro, Arch. Dermat. & Syph. **31**:316 (March) 1935.

5. Pollitzer, S.: Statistical Report of American Dermatological Association, J. Cutan. Dis. **32**:313 (April) 1914; **36**:294 (May) 1918.

6. Crocker, H. R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1405.

"FOLLICULITIS KELOIDALIS" A BETTER TERM THAN "DERMATITIS PAPILLARIS CAPILLITII"

HOWARD FOX, M.D., NEW YORK

For a long time I have felt that the name of the disease originally given by Kaposi to folliculitis of the neck was not only unwieldy but also incorrect. The term "papillaris" is not so exact as folliculitis, and the term "capillitii" is not correct, as many of the lesions are not confined to the scalp. Furthermore, there are apparently few dermatologists who can both spell and pronounce Kaposi's name correctly.

I am especially interested in the change of name to "folliculitis keloidalis," to which the word "nuchae" can be attached if desired. I proposed the change of name when serving as chairman of the committee on classification at the Ninth International Congress of Dermatology in Budapest, Hungary, in 1935. It was unanimously accepted by this committee. Furthermore, the new term is used in the last two editions of the "Standard Nomenclature of Disease and Standard Nomenclature of Operations," a book that should be followed by all American authors.

UNDECYLENIC ACID IN THE TREATMENT OF MONILIAL VULVOVAGINITIS

RODNEY F. KENDALL, M.D., ST. PAUL

Since patients object to the staining properties of methylrosaniline chloride, a search was made for a more elegant and effective method in the treatment of moniliasis. Undecylenic acid with its zinc salt was selected because of previous satisfactory experiences in treatment of monilial dermatomycosis.[1]

REPORT OF A CASE

History.—Mrs. R. M. P., aged 35, was first seen Nov. 28, 1945, complaining of an itching, burning, painful eruption of the vulva and adjacent region of the abdomen and thighs, present for eight months. Diabetes mellitus, present for four years, was fairly well controlled by insulin.

Examination.—Acute inflammation, edema, vesiculation, maceration and fissuring were seen on the vulva and the crurolabial folds with a dry erythematous eruption on the upper third of the medial aspect of the thighs and on the lower portion of the abdomen. The border of the eruption was sharply demarcated. A purulent discharge exuded from the vagina.

Laboratory Examination.—Monilia albicans was found on culture.

Treatment.—Because of catamenia specific treatment was delayed for ten days. Wet compresses of copper and zinc sulfate were used on the skin with only slight improvement; no treatment was used in the vagina.

When the menses ceased, a cleansing douche of tap water was prescribed to be followed by application of 2.5 per cent undecylenic acid and 10 per cent zinc undecylenate in a base of equal parts of vanishing cream [2] and lubricating jelly.[3] The medication was applied in quarter ounce (7.1 Gm.) doses daily into the vagina by means of a contraceptive device. The same cream was applied to the affected skin twice daily.

By the third day there was no discharge; by the fifth day all discomfort was gone, and at the end of a week involution of the eczema was taking place. Subsequent cultures were negative for Monilia.

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1. Shapiro, A. L., and Rothman, S.: Undecylenic Acid in Treatment of Dermatomycosis, Arch. Dermat. & Syph. **52**:166 (Sept.) 1945.

2. The preparation used was Desenex Ointment, Wallace and Tiernan Products, Inc., Belleville, N. J.

3. The preparation used was K-Y Jelly, Johnson and Johnson, New Brunswick, N. J.

COMMENT

The base of vanishing cream and tragacanth jelly spread easily into the rugae at body temperature without becoming fluid. The preparation was stainless and washed off easily. By this method the patient could apply the medication daily herself, thus reducing the number of necessary office visits. In the vagina one daily application of the medication with low concentration of active ingredients was effective probably because it was placed at the site of infection, where it remained until it was washed off.

While no deductions can be made from 1 case, this report shows a simple unobjectionable method of treatment of monilial vulvovaginitis.

SUMMARY

A case of monilial vulvovaginitis was seen in which there was prompt response to applications of undecylenic acid in a vanishing cream and lubricating jelly base by means of a contraceptive device. In this case the method was effective, the number of office visits was reduced, and unpleasant staining by aniline dyes was eliminated.

1160 Lowry Building.

News and Comment

DEATHS

Dr. Erich Urbach died in Philadelphia on Dec. 17, 1946.

GENERAL NEWS

American Board of Dermatology and Syphilology.—At the meeting of the board in Cleveland Dec. 5, 6 and 7, 1946, the following forty-seven candidates were voted certificates by the Board and may now be referred to as certified specialists: James Bagby, St. Louis; Maurice C. Barnes, Waco, Texas; Robert Brandt, Cincinnati 2; Melvin Brody, Cleveland 6; Lewis Capland, Miami Beach, Fla.; Theodore M. Cohen, St. Albans, Long Island, N. Y.; Adolph Conrad Jr., St. Louis; William L. Dobes, Atlanta, Ga.; Hans Field, New York 57; James Murlin Flood, Sayre, Pa.; Paul V. Graham, Wheeling, W. Va.; Joseph Hahn, New York; Vernon Medd Henington, New Orleans; James Bernice Howell, Dallas 1, Texas; Samuel J. Jelso, Albuquerque, N. M.; Joseph Kanter, Chicago; Floralou Kettenbach, Los Angeles; William Leslie Kirby, Winston-Salem 3, N. C.; Joseph Bart Klein, Canton 1, Ohio; Abner Kurtin, New York; John W. Lentz, West Philadelphia; Camillo Benedict Locasto, Brooklyn 15; Irwin Irville Lubowe, New York 24; Katherine MacEachern, Los Angeles; Richard Campbell Manson, Richmond, Va.; Frank M. McDonald, Akron, Ohio; Lee Davidson McLean, New Orleans; Kate Freeman Miller, Corona, N. Y.; Samuel Monash, New York; Leslie Krow Mundt, New Orleans; Meyer Louis Niedelman, Philadelphia 3; Henry Harris Perlman, Philadelphia; Samuel R. Perrin, Pittsburgh; William Lannan Poole, Birmingham, Ala.; Arthur G. Pratt, Camden, N. J.; Harold Price, Chicago; Aaron J. Reiches, St. Louis; Norbert Pierce Ringelman, Albany, N. Y.; Jeremiah E. Ryan, Binghamton, N. Y.; Carl Stevens Sawyer, Providence 6, R. I.; Ira Leo Schamberg, Jenkintown, Pa.; Louis Cotton Skinner, Washington, D. C.; William J. Sweeley, Livingston Manor, N. Y.; Louise Erma Tavs, Chicago 2; Erich Urbach, Philadelphia; Ilona Vass, New York 28, and William David Wolfe, Baltimore.

The following thirteen candidates were also successful in the examinations and will become certified specialists when they have fulfilled the requirement of five years of training and experience in the specialty: David N. Alcon, Los Angeles; Edmond Edelson, Newark, N. J.; Helen Reller Gottschalk, St. Louis 3; Arnold Henry Gould, Washington 6, D. C.; Neville Kirsch, Hartford, Conn.; Beatrice Hart Kuhn, Durham, N. C.; Walter C. Lobitz Jr., Rochester, Minn.; Betty Brachner Owens, Ann Arbor, Mich.; Don Ralph Printz, Cleveland; Morris Jacob Rothstein, Brooklyn 26; Donald Merrill Ruch, Milwaukee; June Carol Shafer, New York, and Ruth Zuckerman, Brooklyn.

The next oral examination to be conducted by the American Board of Dermatology and Syphilology is scheduled for April 25 to 27, in New York. The written examination for group B will be held in various cities in the United States on March 24, 1947. The last date for receiving applications is Feb. 17, 1947.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

BISMUTH IN THE TREATMENT OF SYPHILIS. N. S. VEDROV, Am. Rev. Soviet Med. **3**:106 (Dec.) 1945.

In an attempt to link absorption and elimination of bismuth with the curative process, daily studies were made of the elimination of bismuth injected into patients during the initial and subsequent courses.

It has been proved that only bismuth which is in free circulation is of value in the treatment of syphilis. Since the kidneys pick up the bismuth from the blood and excrete it in the urine, the level of concentration of bismuth in the blood can be determined by measurement of the elimination of the drug. There are three criteria for estimating the therapeutic activity of bismuth by its elimination: 1. Uniform excretion must be maintained at a high level between injections. 2. Elimination must extend over a long time. 3. Excretion must be maintained at a high daily level to correspond with a high level of bismuth in the blood. It becomes clear that the higher the amount of bismuth excreted during treatment and rest, the higher the amount of active bismuth in the body.

Experiments on rabbits indicated that about 70 per cent of the initial dose of bismuth was absorbed from the thigh muscle if the muscle had not been previously injured by injections of bismuth. In those rabbits into whose thigh muscles bismuth had been previously injected, only 34 per cent of the bismuth was absorbed. It is deducible that with increased injection of bismuth there is gradually decreased absorption in ratio to the amount injected.

The amount of bismuth excreted by human subjects was measured. The excretion of the metal in the urine in fourteen days was 35 per cent for those who had not had bismuth previously injected, and approximately 13 per cent for those who had had prior injections of the drug.

The amount of bismuth excreted in the urine after one course of treatment up to one month prior to the start of the second course was 31.6 per cent. With subsequent courses of bismuth the elimination of the drug dropped to 14 per cent of the amount injected as compared with 32 per cent in the first course.

The author concluded that even if small amounts of bismuth were gradually absorbed from the bismuth depots caused by repeated injections, they did not provide enough mobile bismuth for effective treatment, and that a more effective method of bismuth therapy in syphilis must be found, particularly for the bismuth which is to be introduced after the first course.

ANTI-RETICULAR-CYTOTOXIC SERUM IN CHRONIC SKIN ULCERS. L. N. MASKELLEISON, Am. Rev. Soviet Med. **3**:443 (June) 1946.

Thirty-one patients with chronic ulcerations were treated with antireticular cytotoxic serum. These ulcers fell into four general groups: (1) chronic posttraumatic purulent ulcers of the leg, (2) varicose ulcers, (3) gangrenous ulcers of the leg with thrombophlebitis and (4) ulcers due to roentgen irradiation.

Antireticular cytotoxic serum was used at first without supplemental therapy. When it became evident that results were unsuccessful the serum was supplemented with local applications of plasters. The serum was injected at two day intervals in doses of 0.03, 0.06 and 0.075 cc. Occasionally a fourth dose of 0.1 cc. was added.

Of these 31 patients, 13 were completely cured in fourteen to forty days. Of these 13, 6 received the serum exclusively and 7 received the serum supplemented with local therapy. Nine patients showed improvement and in 7 no perceptible

improvement could be discerned. Especially striking results were seen in 2 patients who had roentgen ulcerations.

Experience showed that prerequisite to success in old pyogenic ulcers was a débridement with removal of necrotic tissue.

In general, indications for the use of antireticular cytotoxic serum must be decided for each individual case together with the proper dosage required. The successful use of the serum depends on the correct interpretation of the tests for determining functional conditions of the physiologic system of connective tissue. Four tests were employed, but the test with trypan blue (sodium salt of toluidin-diazodiaminonaphtholdisulphonic acid) was especially valuable. It is based on the size, spread and disappearance of the blue wheal. The coefficient of the cutaneous test is the relationship of the square of the radius of the wheal, after twenty-four hours, to the square of the radius of the wheal immediately after injection of 0.2 cc. of 0.5 per cent solution of trypan blue. The normal coefficient is 15.0 to 18.0. A coefficient of 10 or less indicates disturbance of the physiologic system of the connective tissue.

ROBINSON, Washington, D. C.

TROPICAL ULCER IN GUATEMALA. ALFRED GOLDEN and PADILLA B. ENRIQUE, Arch. Path. **41**:612 (June) 1946.

The authors describe the pathologic, bacteriologic, mycologic and clinical aspects of tropical ulcer as observed in Guatemala. Of the visible pathologic changes none stands out so clearly as the vascular. The significant lesion appeared to be widespread damage of the venous and arterial supply of variable anatomic type but consistently resulting in stenosis. Golden and Padilla were unsuccessful in their search for the factors productive of the vascular changes.

Bacteriologic and mycologic investigation of the 24 patients led to the conclusion that the micro-organisms isolated were harbored by the lesions but were not etiologically related. Dietary factors did not appear to be significant. The predilection for involvement of the lower extremities is explained by the authors as due to the consequences of vascular insufficiencies, whether these are produced by low temperatures, occlusive arteriosclerosis or failure of adequate venous return.

The therapy of tropical ulcer has been directed toward bacterial stasis or antisepsis, without great success. It would appear that methods aimed at restoring the adequacy of the blood supply of the leg would prove more fruitful therapeutically.

ETIOLOGIC CONCEPTS AND PATHOLOGIC ASPECTS OF AINHUM. B. H. KEAN and HAROLD A. TUCKER, Arch. Path. **41**:639 (June) 1946.

Kean and Tucker point out that theories regarding the cause of ainhum may be grouped under three general headings: infectious, constitutional and mechanical. In Panama they observed a dozen cases and reviewed the records of 45 persons. Microscopic studies were carried out in 6 cases showing that the inflammatory reaction is not extensive, and the authors find difficulty in conceiving how the reaction which is so ill defined microscopically could possibly produce the lesion which is so distinctive grossly. While they are unable to offer any positive explanation, they think that the groove or burrow at the digitoplantar fold is not caused by a constricting band of fibrous tissue. Neither are they impressed by the recent suggestion that chronic osteomyelitis is the essential lesion of ainhum.

DEVELOPMENT OF SEBACEOUS GLANDS FROM INTRALOBULAR DUCTS OF THE PAROTID GLAND. PHILIP H. HARTZ, Arch. Path. **41**:651 (June) 1946.

After studying a case of tumor of the parotid gland Hartz presents some interesting photomicrographs showing epithelial formations which could not be distinguished from small sebaceous glands. He states that these cells were easily differentiated from the acinous cells of the parotid gland. Since the parotid gland develops from the ectoderm on the deep aspect of the cheek and sebaceous glands

are known to appear in that region during puberty, the author thinks that the development of sebaceous glands from the duct of the parotid gland cannot be considered as strange.

LYNCH, St. Paul.

PROTECTIVE SKIN COATINGS FOR THE PREVENTION OF SUNBURN. MATTHEW LUCKIESH, A. H. TAYLOR, H. N. COLE and TORALD SOLLMANN, J. A. M. A. **130**:1 (Jan. 5) 1946.

Erythema or burn as a result of exposure to natural sunlight is principally caused by ultraviolet energy in the spectral range 2,900 to 3,200 wavelengths. Dark Red Veterinary Petrolatum (Standard Oil Company of New Jersey) was found to be quite opaque to erythemal energy. The compound is not irritating and adheres tenaciously to the skin. Phenyl salicylate was also found to provide excellent protection against ultraviolet radiation when put up in a 10 per cent cream. Titanium dioxide is not a dependable protective agent. Zinc oxide is of definite value in preventing sunburn. Menthyl salicylate was not a particularly good agent, nor was "Sunex" ointment (Abbott Laboratories, Chicago) containing butesin, metaphen and oleic acid ester amide diethylamine in cold cream.

HENSCHEL, Denver.

THE SPECIFICITY OF SEROLOGICAL PRECIPITATION. FRANK LANNI, J. Exper. Med. **84**:167 (Aug.) 1946.

Earlier observers have reported that the process of serologic precipitation is a sequence of two phases: a rapid primary phase involving a combination of antigen and antibody molecules and a slower secondary phase in which the initial molecular complexes aggregate. The progress of the second phase is typically manifested in the development of opalescence and in the formation and sedimentation of macroscopic particles of precipitate. After experiments with a turbidimeter and a dark field microscope Lanni thinks that serologic precipitation is largely governed by a highly specific mechanism except in the terminal period, when the operation of nonspecific forces becomes apparent. Recognition of the multiple morphologic character of specific precipitation allows a simpler description of the process. The union of antigen and antibody results in primary molecular complexes which may then combine with each other or with free antigen and antibody molecules. As larger and larger molecular complexes are elaborated they are detectable in the dark field as minute light-scattering particles, seromicrons, which continue to grow. These seromicrons are regarded as elementary particles of specific precipitation.

LYNCH, St. Paul.

THE ELIMINATION OF HUMAN REACTION-PRODUCING MATERIAL FROM HORSE-DERIVED ANTISERUMS: AN ELECTRICAL METHOD. EUGENE CARDONE, J. Lab. & Clin. Med. **31**:829 (Aug.) 1946.

Treatment with immune serum has been associated with certain serologic reactions which have done much to discourage its use.

The aim, in the past, has been to eliminate all immunologically inert protein from serums in hope that the reaction-producing substance would go with them. This has been done by processes of purification and concentration.

The author describes an electrical process followed by six days of dialysis which he used to reprocess antimeningococcus serum by the water precipitation method.

The electric process frees the reaction-producing material and dialysis changes its form so that it is eliminated or inactivated.

These procedures eliminate from purified and concentrated horse-derived antiserum substances which cause immediate serologic reactions when injected in man without lowering the antibody potency per unit of protein nitrogen.

GELBER, Los Angeles.

THE POSSIBLE INTER-RELATION OF PSORIASIS AND STREPTOCOCCUS FAECALIS. J. H. SWARTZ, New England J. Med. **233**:296 (Sept. 16) 1945.

From the observation of sensitivity to intradermal injections of minute amounts of an autogenous vaccine made from a certain strain of Streptococcus faecalis in cases of psoriasis and the fact that no Str. faecalis is found in Negroes, most of whom do not suffer from psoriasis, Swartz suggests a possible relationship between Str. faecalis and psoriasis.

RONCHESE, Providence, R. I.

THE EFFECT OF UREA, URETHANE AND OTHER CARBAMATES ON BACTERIAL GROWTH. LOUIS WEINSTEIN and ALICE MCDONALD, Science **101**:44 (Jan. 12) 1945.

This investigation was carried out to determine the antibacterial properties of the carbamates against numerous gram-negative and gram-positive organisms.

The results indicate that ethyl carbamate (urethane) and urea exert both a bacteriostatic and bactericidal action mainly against gram-negative bacteria and to a lesser degree against gram-positive organisms. It was also found that they antagonize sulfonamide inhibitors and increase the solubility of sulfonamide compounds. Evidence was obtained which indicates that ethyl carbamate does not impede healing of wounds. The activity of the four carbamate compounds tested appears to be in the following order: Most active is butyl carbamate, and least effective is urea, with ethyl carbamate and propyl urea occupying a middle ground.

A small number of infections were treated with a mixture containing 10 Gm. of ethyl carbamate and 1 Gm. of sulfanilamide in 100 cc. of water, and those in which gram-negative bacteria were predominant responded rapidly, with sterilization and healing of the wounds.

A SEARCH FOR VIRUS-INACTIVATING SUBSTANCES AMONG MICROORGANISMS. DORIS JONES, F. R. BEAUDETTE, WALTON GEIGER and SELMAN WAKSMAN, Science **101**:665 (June 29) 1945.

One hundred and fifty organisms, comprising bacteria, fungi and actinomycetes, were tested for antiviral activity in vitro against the viruses of fowl pox and laryngotracheitis.

Three organisms, a strain of actinomyces antibioticus, trichoderma sp. and actinomyces sp. were found to have a definite inactivating effect. The active principle of one of these organisms was actinomycin A, which is known to be highly toxic to animals. The inactivating effect of the other two organisms was less extensively studied; no claims regarding their antiviral potentialities can be made at present.

THE EFFECT OF PENICILLIN IN EXPERIMENTAL RABBIT SYPHILIS. GEORGE W. RAIZISS, Science **102**:329 (Sept. 28) 1945.

This article reports on the final results obtained by removing the popliteal lymph nodes one hundred to one hundred and fifteen days after the testicles of penicillin-treated rabbits became normal. These nodes were tested for spirochetes by being intratesticularly transferred into healthy rabbits, which were observed for three months for evidence of infection.

The schedule of dosages carried out was as follows: (1) One syphilitic rabbit received 2,500 Oxford units of penicillin in aqueous solution intramuscularly twice each day for eight days, for a total of 40,000 units per kilogram of body weight; (2) two rabbits received intramuscular injections of 5,000 Oxford units of penicillin in oil suspension once each day for eight days, for a total of 40,000 units per kilogram of body weight; (3) one rabbit received 3,300 Oxford units three times daily for eight days, for a total of 79,200 units per kilogram of body weight, and (4) two

rabbits received 5,000 Oxford units of penicillin in oil suspension twice a day for eight days, for a total of 80,000 units per kilogram of body weight.

The results of the experiment reveal that the rabbits which received 40,000 Oxford units per kilogram of body weight in a period of eight days, whether the drug was in aqueous solution or in oil suspension, were completely cured of syphilis. Translated into a treatment schedule for a patient weighing 60 Kg., the total dose would be 2,400,000 units. It was also noted that in the animals receiving twice the dose, namely, 80,000 units per kilogram of body weight, the lesions cleared much faster.

BAL (BRITISH ANTI-LEWISITE). L. L. WATERS and CHESTER STOCK, Science **102**:602 (Dec. 14) 1945.

An antiarsenical, 2,3-dimercaptopropanol, called Bal (British Anti-Lewisite), an agent effective against several arsenical war gases, has been found of therapeutic value in certain cases of arsenical poisoning encountered in civilian medicine.

Dimercaprol is not an innocuous substance inasmuch as profound toxic effects —for example, apathy, lacrimation, blepharospasm, conjunctival edema, salivation, vomiting, muscle tremors, convulsions, coma and death—have been noted in animals to which it had been administered. These striking physiologic and metabolic changes are not accompanied by comparable morphologic alterations. In the skin it causes localized erythema and edema, but to mucous surfaces it is extremely irritating, producing severe edema and ulceration.

In man, solutions or ointments or sterile peanut oil–benzyl benzoate solutions (for intramuscular injections) containing 5 to 10 per cent dimercaprol are well tolerated. Inunction of a total of 1 cc. of undiluted dimercaprol or of 2 Gm. in a jelly base also fails to produce toxic effects.

Of more than 200 patients treated in the United States and England, the majority have had either arsenical dermatitis or hemorrhagic encephalitis after the administration of oxophenarsine hydrochloride. Included, however, are some patients who had massive overdoses of arsenical drugs and other less common manifestations of arsenical poisoning. The available data strongly suggest that this drug is effective in such cases and probably is of value in some cases of blood dyscrasia resulting from arsenotherapy. It appears to be of no value in cases of so-called arsenical jaundice.

In addition it has been given a preliminary clinical trial in the treatment of mercurial poisoning, and the results have been most encouraging.

RODIN, South Bend, Ind.

GENERALIZED VACCINIA. N. G. NOJUMDAR, Calcutta M. J. **41**:290 (Aug.-Sept.) 1944.

Generalized vaccinia is a well recognized complication of vaccination and is considered to be one of the most serious. The death rate is high. The author reports a case of generalized vaccinia in a Hindu boy 2 years old. The patient presented a generalized vesicopustular eruption which began about two weeks after primary vaccination. Sulfonamide therapy resulted in complete involution of the lesions within four days. The author quoted statistics giving the incidence of generalized vaccinia as varying from 1 in 39,484 vaccinations to 1 in 96,756. The fatality rate was 11.7 per cent. The following points must be satisfied to diagnose generalized vaccinia: 1. Autoinoculation should be excluded. 2. The eruption must appear not earlier than the fourth and seldom earlier than the ninth day after vaccination. 3. The eruption must be elsewhere than in the neighborhood of the site of vaccination. 4. There must be a vesicular stage.

The pathogenesis of generalized vaccinia is poorly understood. It has been suggested that the skin produces immune bodies at the site of vaccination and if the skin fails to elaborate a sufficient amount of antibodies the virus enters the

body unmodified and produces systemic reactions. Complications of vaccination occur most frequently if primary vaccination is delayed later than 1 year and vaccinia is most apt to occur in those who have eczema, impetigo or other cutaneous diseases. The case which the author reports indicates that the sulfonamide compounds demand further trial in the treatment of vaccinia.

LAYMON, Minneapolis.

LYMPHOGRANULOMA VENEREUM FROM AN IMMUNOBIOLOGIC POINT OF VIEW. S. HELLERSTRÖM, Acta dermat.-venereol. **21**:222 (Feb.) 1940.

The skin of persons with lymphogranuloma venereum shows specific hypersensitivity to the intracutaneous injection of the contents of circumscribed broken-down buboes from this disease. This test, known as the Frei test, becomes positive in one week to two months after the appearance of the inflammation of the lymph nodes and may remain positive for as long as thirty-one years. Consequently, a positive Frei test denotes only that a patient has or has had the disease. It has not been possible to sensitize healthy persons to the Frei antigen; therefore, as far as one can judge, the test is specific.

If chancroid or early syphilis coexists with lymphogranuloma venereum, there may develop an anergy of the skin (Frei). However, the apparent anergy may be due to a delay in the development of the sensitivity to the Frei antigen, and this delay may be responsible for the anergy in patients with the mixed infections cited by Frei. In view of this it must be remembered that a negative Frei test, even after a rather long period, does not exclude the presence of lymphogranuloma venereum infection. The testing must be continued. Side reactions, such as erythema nodosum, fever and inflammation of the previously infected inguinal lymph nodes, have been observed. In the cases in which erythema nodosum appeared vesicles on these lesions were produced with cantharides, and the fluid obtained from these vesicles was tested intracutaneously on persons known to have lymphogranuloma venereum and on controls. There were positive Frei reactions in the infected patients and negative reactions in the controls.

As to treatment, the intravenous injection of Frei antigen yields better results than all other methods. The best results were obtained in the cases of glandular infection and the poorest in those of rectal infection. Following intravenous injections of the antigen, there was a sharp rise in body temperature 40 C. (104 F.) or more. On repeated injections, the temperature rises less and less until it eventually remains normal, irrespective of the amount of antigen used. This seems to indicate progressive desensitization. Rarely, with this method of therapy acute and intense symptoms appear resembling an anaphylactoid reaction.

SKIN LESIONS DURING THE COURSE OF ULCERATIVE COLITIS. I. R. JANKELSON and C. W. MCCLURE, Acta dermat.-venereol. **21**:255 (March) 1940.

Seven cases of chronic idiopathic ulcerative colitis complicated by infection of the skin are presented. In all these cases infection of the skin developed at the height of an acute exacerbation, and there was active diarrhea with watery stools containing mucus, blood and pus. The cutaneous lesions varied a great deal in severity. In some cases they were merely punched-out ulcers or redness, swelling and induration without abscess formation. In other cases they were multiple distinct abscesses. The bacteria isolated from some of these cutaneous lesions were found to be identical with bacteria isolated from some of the ulcers in the intestinal mucosa in 2 of 3 cases. These organisms were Staphylococcus aureus, Staphylococcus albus, hemolytic streptococci, Bacillus pyocyaneus and Bacillus coli, either separately or together. In spite of these findings it was felt that lowered resistance to infection rather than metastasis played the important etiologic role in the ulcerations of the skin. Improvement of the cutaneous lesions accompanied improvement of the colitis. Treatment was directed at the colitis, with symptomatic treatment of the cutaneous lesions.

TREATMENT OF EPIDERMOPHYTOSIS ON THE EXTREMITIES WITH IONTOPHORESIS OF COPPER. O. JERSILD and M. PLESNER, Acta dermat.-venereol. **21**:268 (March) 1940.

Fifty-eight patients with dermatophytosis were treated by iontophoresis of copper. An almost constant effect of the treatment was a subsiding of the pruritus after the first or the second treatment. The denuded, oozing areas dried up and were gradually covered with normal epithelium. On the average treatment was completed after two to five applications. Fifteen per cent received from eight to eleven applications. In four to twelve months there was no relapse in 85.7 per cent of all patients. The authors claim the following advantages from this method of treatment: (1) Itching is promptly alleviated; (2) cure is effective and rapid; (3) iontophoresis is simple, painless and clean, and (4) there is no injurious effect on normal skin.

THE FINSEN TREATMENT AND ITS SIGNIFICANCE TO RATIONAL COMBATING OF LUPUS VULGARIS. SVEND LOMHOLT, Acta dermat.-venereol. **21**:280 (March) 1940.

Lomholt states that with his modern Finsen apparatus it is practicable to raise the percentage of patients recovered from lupus vulgaris to nearly 100, provided treatment is started at an early stage and continued until maximum results are obtained. The treatment may be local, with cutaneous pressure, or it may be generalized with Finsen light baths. The important factor of this new lamp (Universal) is the elimination of the infra-red rays which is accomplished by means of filters and a new type of carbons.

One hundred and ninety-six patients were treated during the period 1924 to 1936. Of 181 patients, 175 were completely cured of the disease at the time of writing. The Finsen lamp treatment may be characterized as a therapeutically effective and cosmetically excellent method.

MYCOSIS FUNGOIDES. A. POULSEN, Acta dermat.-venereol. **21**:365 (March) 1940.

After a description of mycosis fungoides in all its forms, 13 cases of the disease are reported. In 4 of these cases the disease was of the classic Alibert-Besnier type. In 5 cases it was of the inverse type, characterized by the appearance of tumors initially, which then are followed by a polymorphous exanthema or a generalized erythroderma. The disease in 3 cases was of the d'emblée type, and in 1 case it was cured in the premycotic stage.

The duration of the disease prior to admission was one to fifteen years. In 6 of the cases which were fatal the duration was two to eight years. The localities of the lesions were in order of their frequency: (1) the scapular region (6 of 13 cases), (2) the face, and (3) the trunk and the proximal parts of the extremities.

In many of the cases the mycotic infiltration extended right up to the epidermis, leaving no free margin just beneath the epidermis such as is usually described. All patients were given roentgen ray treatments in larger doses than were necessary to clear the lesions, in order to avoid having to irradiate at a later date skin previously irradiated and possibly resistant to radiation.

Six of 13 patients died, including 3 in whom the eruption was universal. Three patients were symptom free four years after being treated with roentgen rays. The remaining patients improved but continued to have small relapses.

In 1 case the patient presented, on roentgen examination, irregular destructive clearings in both femurs, about the size of hens' eggs, which resembled destructive tumor metastatic processes in the bones. In another case roentgenograms taken one month prior to death showed massive spots in the lower half of each lung field and enlargement and blurring of the hilar shadows. These abnormalities were interpreted as mycotic infiltrations, and this interpretation was verified at autopsy.

In conclusion Poulsen emphasized the importance of energetic roentgen ray treatment administered from the start. The physician must not be satisfied by the rapid reduction in the extent of the morbid change after the application of radiation

but must be guided by the established experience that subsequent rational irradiation is far less effective than the same treatment would have been if it had been employed initially.

CUTANEOUS MANIFESTATIONS OF LYMPHOGRANULOMATOSIS BENIGNA (SCHAUMANN). E. B. VOSBEIN and P. BONNEVIE, Acta dermat.-venereol. **21**:408 (March) 1940.

A detailed clinical, morphologic and histologic description of lymphogranulomatosis benigna (Schaumann) is presented. The authors based their diagnoses on histologic observations and on little or no sensitivity to tuberculin as well as on the presence of demonstrable internal manifestations in lungs, bones, tonsils, nasal mucous membranes or conjunctivas. From a morphologic point of view the cutaneous lesions can be divided into typical forms (i. e., nodular, nodose and diffusely infiltrating forms as described by Boeck and Besnier) and nontypical forms. Of the patients with nontypical forms of lesions some had lupus-vulgaris-like lesions; some presented angiolupoids; some had annular forms; some had sarcoids localized in old scars, and others presented lesions resembling erythema nodosum, lupus erythematosus and psoriasis.

In all of the nontypical forms the histologic examination revealed superficial infiltrates in the corium, frequently accompanied with hyperkeratosis, parakeratosis and keratotic follicular pegs. In addition, pronounced necrosis was always present.

Of the internal manifestations, pulmonary lesions were present in about one-half the cases, lesions of the nasal mucosa in one third and osseous lesions in one fifth.

The authors express the opinion that the cutaneous manifestations of Schaumann's disease do not constitute a well defined clinical picture. In only about one half of the cases have there been typical sarcoids of Boeck and lupus pernio of Besnier. The other forms have probably in the past been classified as nontypical tuberculosis of the skin.

THE EPIDEMIOLOGY OF SCABIES WITH PARTICULAR ATTENTION TO ITS RELATIONSHIP TO VENEREAL DISEASE. T. E. OLIN, Acta dermat-venereol. **23**:14 (Feb.) 1942.

There is a sharp increase in the incidence of scabies after puberty. In women it is most frequent in the age group of 16 to 20 years and in men between the ages of 21 and 25. Only 14 per cent of scabies appears after 35 years of age. Venereal diseases appear in similar age groups and present parallelism as to seasonal fluctuations. The greatest incidence appears between September and November, and the least number of cases appear in June and July.

The periodic fluctuations do not run a parallel course in scabies and venereal disease. With a decrease in living standards there is an increase in prostitution and cramped housing conditions, which leads in turn to an increase in scabies. However, at least in Helsinki, the incidence of venereal disease increases with a crescendo in economic prosperity.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

A. Fletcher Hall, M.D., *Chairman*

Clement E. Counter, M.D., *Secretary*

May 8, 1945

Epithelioma in Lupus Vulgaris (Presented for Therapeutic Suggestions).
Presented by DR. A. FLETCHER HALL.

W. P. is an unmarried woman aged 82 years. About sixty years ago she was told that she had pulmonary tuberculosis. She moved to the South from Kentucky and later to the West, for her health. She has been well since moving to the West twenty-three years ago.

At the same time that tuberculosis was diagnosed, a small lesion of the skin behind the lobe of the right ear was diagnosed as lupus vulgaris. It was treated with the cautery, but it recurred and spread forward and upward, destroying the lobe of the ear. About 1900, the then existing area of involvement at the angle of the right jaw was treated with roentgen rays. No progression of the disease was seen until she came to California twenty-three years ago. There was no superimposed neoplastic growth until July 1944, when the lesion on the right temple appeared. The lesion on the right side of the mouth appeared about two months later. She has not sought treatment because she believed that the cutaneous abnormality was a roentgen ray burn.

The patient is a slender, elderly woman in good possession of her faculties and apparently well. She suffers from hypertensive cardiac disease.

The entire right side of the face and upper part of the neck, from the anterior margin of the ear to the outer canthus of the eye, the right nasolabial fold and the right half of the chin are involved in a plaque consisting of closely set, purplish red, sessile, split pea-sized papules. The borders of this area are well limited and extend just across the midline of the front of the neck. Diascopy shows the so-called apple jelly appearance of nodules. The lobe of the right ear and adjacent portion of the cheek below and anterior to the ear are atrophic and blanched and have none of the red papular lesions. Just lateral to the lateral margin of the bony orbit of the right eye is an oval, abruptly elevated, pale pink tumor, the size and shape of a biscuit, with an irregular surface and accentuated border. Just lateral to the right commissure of the mouth is a similar but smaller neoplastic mass.

DISCUSSION

DR. CLEMENT E. COUNTER: This woman truly presents a most striking picture, and I believe that there is no doubt that she has lupus vulgaris and that she also has rather large epitheliomas within the area of involvement with lupus vulgaris. When one notes her age and state of health as suggested by the history, one may consider not doing any treatment whatever. Probably she will die of hypertension before her cutaneous disease becomes fatal. However, when one realizes that she has been here much longer than we have one knows that she has survived many of the hazards of younger life and that she may die of other causes if the more aggressive cutaneous lesions are treated. I should suggest no particularly active treatment for the lupus vulgaris but that suitable roentgen rays be used for the epitheliomas. I realize that this would not be good therapy for a younger person, but I consider it the best for this woman.

DR. HAL E. FREEMAN: A biopsy might do some good. If this is a malignant condition and contains a lot of mitotic figures then use of roentgen rays might be indicated, and if it is not that type of disease then both the lupus vulgaris and the epitheliomas could be cauterized and curetted.

DR. M. E. OBERMAYER: I agree with Dr. Counter's suggestion to treat the carcinoma by means of roentgen rays only if definite information can be obtained that this area has not been previously treated by the same modality for lupus vulgaris.

DR. A. FLETCHER HALL: The roentgen ray treatment she received was in 1900, and she says that her whole face except the small area involved at that time was covered with lead sheets. As far as I can make out, the area treated was the angle of the right jaw, which is nearly all scar tissue. The part now involved with neoplasms, therefore, was covered with lead when she had the original treatment for the lupus.

DR. NELSON PAUL ANDERSON: Actually, epitheliomas developing on lupus vulgaris were reported long before the roentgen ray was discovered. I cannot feel that any roentgen ray therapy she received in the past had anything to do with the development of these two epitheliomas.

DR. A. FLETCHER HALL: She was told that this was all due to a roentgen ray burn. That is why she would not have anything more done about it.

DR. SAMUEL AYRES JR.: I think that the question of therapy brings up an interesting point. I do not think that this patient is too old for treatment. I think that it would probably be perfectly possible to remove these areas *in toto* with the patient under local anesthesia, with the epinephrine left out of the procaine hydrochloride if desired. I do not recall enlarged glands in her neck, and if there were not I think that one should attempt total removal of each individual epithelioma. They are undoubtedly composed of prickle cells. I think that it is always safer to use the cutting current than to try to treat them by irradiation.

DR. ANKER K. JENSEN: I agree with Dr. Ayres in advising electrosurgical removal of epitheliomas. I do not think that the surgical shock would be so great as that with roentgen rays.

DR. H. C. L. LINDSAY: May I suggest use of radium for treatment of the cancer and heavy exposures of water-cooled ultraviolet rays (contact compression) for the lupus vulgaris (Lindsay, H. C. L.: Intensive Water Cooled Quartz-Light Therapy, *Urol. & Cutan. Rev.* **29**: no. 9 [Sept.] 1925)?

DR. A. FLETCHER HALL: I do not anticipate treating the lupus vulgaris. If it progressed only this far in sixty years, I think that the next ten years will not cause her further trouble. As far as the treatment of the epitheliomas, I should favor irradiation, because of the extreme youth of these lesions. Dr. Freeman well pointed out the idea of taking into consideration what grade of prickle cell carcinoma is present. I think that any prickle cell epithelioma that grows to the size of a teacup in ten months is made up of rapidly dividing cells, and if any prickle cell epitheliomas should be radiosensitive these should.

Superficial Basal Cell Epitheliomas on Psoriasis. Presented by DR. HAL E. FREEMAN.

K. J. is a man aged 47 years. He has had a widespread eruption for twenty-six years. There was an epithelioma on the right side of his nose, which was treated in 1939. In the past, approximately forty roentgen ray treatments were given for the lesions on the anterior and posterior surfaces of the neck. The lesions on the neck have never healed. The anterior one persists, and the posterior one has become an open eroding ulcer.

On the lower right side of the neck, anteriorly, is an erythematosquamous, slightly indurated lesion about 2 by 3 cm. Posteriorly, on the same side of the neck is a similar lesion. A superficial ulcerated circular area about 1.5 cm. in

diameter is in the central portion of this lesion. Erythematopapulosquamous lesions are present on the elbows, knees and lower part of the back.

The cholesterol determination of the blood was 212 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative.

A biopsy specimen showed that the two lesions had similar changes. The posterior one showed ulceration and some hyperkeratosis at the margin of the ulcer. Neither showed a considerable amount of dyskeratotic change or any intraepidermal epitheliomatosis. There are localized accumulations of deeply staining basal cells in the upper part of the cutis of each section.

DISCUSSION

DR. NELSON PAUL ANDERSON: I wish that Dr. Freeman would change the diagnosis to superficial basal cell epithelioma "with" psoriasis instead of "on" psoriasis. I was particularly interested that one cannot secure a history of arsenical ingestion. The patient had no arsenical keratoses that I could find. Nevertheless, he has had psoriasis for twenty-five or thirty years, and it would be rare if some one had not given him a little arsenic. Incidentally, when one tries to secure a history of arsenical administration, the patient may not recall that he ever received arsenic, or he may have been given the drug as a child. I thought that the patient had an excellent cosmetic result in the removal of an epithelioma from the side of his face. The patient did not agree. His mental attitude is antagonistic. I am not convinced, however, that he has not had arsenic at some time in his life. I should like to have some arsenical studies of his urine before and after administration of sodium thiosulfate.

DR. HAL E. FREEMAN: I am glad that Dr. Anderson brought up the question of whether this is malignant growth "on" psoriasis or "with" psoriasis. Frankly, I will not say that histologically this section could be argued to be psoriasis. It is typically a basal cell superficial lesion, and the man gave a history of a psoriatic lesion for many years and then of this lesion developing on it. I must have been influenced by his history in calling it an epithelioma "on" psoriasis. I did not see any telangiectasia around it, and the histologic section did not show any atrophy at all that one could attribute to radiodermatitis. My present plan is to cauterize these lesions and let them heal by granulation and to withhold further use of roentgen rays.

A Case for Diagnosis (Stomatitis Due to Ingested Medication). Presented by DR. CLEMENT E. COUNTER.

H. S. is a woman aged 57 years who has not worked for the past five and one-half years because of an automobile accident which particularly injured her left knee and coccyx. There is still much pain in the lower part of the back and the left leg. There is much insomnia. It is partly due to pain and tenderness of the left leg. To relieve this pain a "nerve block" was accomplished in the hospital three years ago.

Eighteen months ago she began to have "canker sores" in her mouth. These sores were persistent, so that she has had one or more lesions in her mouth all the time. About six months ago she began to have larger vesicular lesions. These contain bloody serous fluid. Some lesions are always present, and one week ago discomfort was severe. It was even painful to drink water. She has lost the sense of taste. Lesions sometimes involve all parts of the mouth, including the gums, the soft palate and the nasal pharynx.

At present two gray-covered excoriated oval lesions are present on the inner surface of the cheeks, opposite the lower third molars. One lesion is present on each cheek. They are about equal in size, being about 6 by 8 mm. in diameter. All lesions have been in the oral cavity. Medicaments taken by her in the past year include vitamin B complex; 1 grain (0.06 Gm.) of thyroid substance daily; a pink-coated tablet containing 0.02 Gm. of phenobarbital, 0.1 mg. of extract

of belladonna and 0.3 mg. of ergotamine tartrate, and "Siblin," which is a psyllium seed product with vitamin B_1.

DISCUSSION

DR. M. E. OBERMAYER: I think that this case illustrates well the disease called necroticum mucosae oris by Scandinavian authors. It is the deepest type of an inflammatory process of which periadenitis mucosae necrotica recurrens and aphthous stomatitis are more superficial forms. Patients with this disease always show signs of nervous instability and exhaustion. These features were undoubtedly present in this patient.

DR. SAMUEL AYRES JR.: I tried to get a history of use of phenolphthalein in this case, without success, but I am still convinced that there may be a drug factor.

DR. A. FLETCHER HALL: In view of the possible connection with aphthous stomatitis, I think that a relatively harmless treatment to try, which might do some good, would be vaccination with smallpox vaccine intradermally, as one would do in treatment of recurrent herpes simplex.

Porokeratosis (Mibelli). Presented by DR. ANKER K. JENSEN.

J. L. is a white woman aged 31 years. A small thickened area started to develop on the right forearm about ten years ago. This has continued until now. It has spread peripherally.

There is a round lesion about 2 cm. in diameter. The central part appears depressed with a firm elevated margin. A slight scaling is on the central part of the lesion.

The biopsy specimen showed much hyperkeratosis, which was greatest around the sweat ducts where they pass through the rete. There was thinning of the deeper portions of the epidermis. Hair follicles and sweat glands were scattered and sparse.

DISCUSSION

DR. SAMUEL AYRES JR.: The disease is extremely rare. I have seen only 1 similar case. The particularly interesting factor is its extreme refractoriness to treatment. I treated my patient with various procedures, including freezing and electrodesiccation, without benefit, and apparently similar treatments have been used in this case, with similar lack of results.

DR. ANKER K. JENSEN: This case is presented because porokeratosis (Mibelli) is not seen frequently in Los Angeles. I expect to remove this lesion by wide deep electrodesiccation.

CHICAGO DERMATOLOGICAL SOCIETY

Frederick R. Schmidt, M.D., *President*

Marcus R. Caro, M.D., *Secretary*

May 16, 1945

Lipid Proteinosis. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. Z. FELSHER.

H. P., a white woman aged 23, was first seen at the University of Chicago Clinics on May 15, 1945. She complained of a peculiar condition of the face and neck, present since babyhood. The patient stated that her trouble began with "infantile eczema," which she had for about seven years. She has been hoarse since babyhood. Her hair has fallen out completely and then regrown on three occasions, the last time when she was 12 years of age. Baldness at that time lasted one month. Three years ago several large nodules appeared on the knees

and elbows. For the past several years the patient has suffered with severe cavities of the teeth, and three years ago all the teeth were extracted. Apparently there were no deformities of the teeth.

The physical examination at this time reveals scanty hair. The face is diffusely and irregularly infiltrated with yellowish nodules and plaques. The neck on its anterior aspect shows several reddish, round, small nodules. The lips, especially the lower, and the buccal mucosa are thickened, hard and rigid. Similarly the tongue is diffusely infiltrated and has a woodlike consistency. In the midline of the dorsum of the tongue there are several hard irregularly shaped nodules. The palate and uvula are thickened and rigid. Laryngoscopic examination shows the epiglottis to be rigid, thick and smoothly infiltrated. Because of the rigidity of the epiglottis, the vocal cords are difficult to see; they are thickened but smooth. The posterior commissure of the larynx shows a whitish, irregular, finely granular surface. The patient is edentulous. The knees and elbows show several large, well circumscribed, infiltrated, reddish brown nodules.

A frozen section with fat stain showed the picture of lipid proteinosis.

DISCUSSION

DR. E. E. STENHOUSE: About a year ago I presented before this society a patient with lipid proteinosis. This patient was about 23 years old. She had many more lesions in the mouth, especially on the tongue and buccal mucosa. She had no lesions on the face. My associates and I made studies of the blood, and the total lipids were within normal limits as far as we could tell. We treated the patient with lipocaic. She was seen at the University of Chicago, where Dr. Dragstedt was working with lipocaic. After several months her voice improved considerably, but the lesions had undergone involution only to a certain point and beyond that there was no further improvement. The patient herself noted that the lower lip, which had been stiff, was more movable, and she had less difficulty in speaking. I see the patient from time to time, and there is no further improvement.

DR. STEPHEN ROTHMAN: About half of the 16 patients reported in the literature had slightly increased serum cholesterol values; those of the others were normal. The disease probably represents a degeneration of the tissues and not a metabolic disturbance. We should like to try lipocaic, but it is not available at present. The patient has such extensive infiltrates that we probably will be able to perform microchemical tissue analysis of the fat.

NOTE.—The fat was extracted from the infiltrate, and the phosphorus content of total fat was found to be 1.13 per cent.

Lichen Planus Annularis (Limited to Eyelids). Presented by DR. CLARK W. FINNERUD.

R. L. R., a married woman aged 45, complained of an itching eruption of the medial half of each upper lid, the eruption on the left of four years' duration and that on the right of six or eight months' duration. She stated that she had always been of nervous temperament but had been less nervous after her artificial menopause four years ago. She stated further that she had had a severely itching patch a few years ago on the left breast and one on the right hip, both of which disappeared with the use of an ointment.

The physical examination reveals a finger nail–sized annular lesion of the medial third of the right upper eyelid and a larger oval one of the medial surface of the left upper eyelid.

DISCUSSION

DR. EDWARD A. OLIVER: I do not believe that lichen planus of the eyelids is extremely rare. I have seen 4 or 5 cases in my own practice, and doubtless many of the others have seen cases. Nevertheless it was a most interesting case.

DR. CARL W. LAYMON, Minneapolis: Dr. Michelson and I have been fortunate in seeing a good many cases of lichen planus of the eyelids. Lesions on the lids may occur alone or with lesions elsewhere on the body. There are three forms of lichen planus of the eyelids: the ordinary papular type is commonest; the annular form, as illustrated by Dr. Finnerud's case, is also occasionally seen. The third form is characterized by reticular pigmentation of the lids which simulates erythema ab igne.

DR. CLARK W. FINNERUD: I do not recall having previously seen lichen planus limited to the lids. It is interesting that here is a disease presumably referable to the nervous system occurring in an area where neurodermatitis limited to the lids is commonly seen. Dr. Sandis and I have seen, within the last week or two, 2 cases of generalized lichen planus, classic cases, associated with classic lichen simplex chronicus, 1 of that on the nucha and 1 of that on both legs. It is interesting to me to see these diseases overlapping.

Juxta-Articular Nodes, Origin Undetermined. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. D. NIEDERMAN.

V. T., a white married woman aged 48, first noticed a small node on the extensor surface of her right elbow sixteen years ago. This was followed by similar lesions on the left elbow. The lesions grew slowly until they were almost walnut sized in the course of five to six years. Later nodes developed on both legs and on the right parietal area of the scalp. Eight years ago all the nodes were surgically removed except the one on the scalp. There was no recurrence of the nodes on the legs, but within one year those on the elbows recurred. The node on the right elbow was removed four times and that on the left elbow twice.

The nodes are not tender, but there are a throbbing pain and weakness present in her right forearm and hand. These symptoms were absent when the nodes were removed. The patient has had no other cutaneous disorders except a series of boils in 1922 and varicose veins.

She had influenza and typhoid fever in 1919 and osteomyelitis of the left tibia in 1919 and 1920. A thyroidectomy was performed five years ago because the patient had a basal metabolic rate of + 20 to 40 per cent and pressure symptoms due to the enlargement of the thyroid gland. She has had night sweats for the past six or seven years but no thoracic symptoms.

The patient denies that she has had any venereal disease. Five years ago she had negative reactions of the blood. Her husband had a negative reaction of the blood four years ago. She has three children, who are healthy, and she has had no miscarriages. There is no evidence that she had congenital syphilis. She has never lived in a tropical country.

The general physical examination shows normal findings. Her blood pressure is 180 systolic and 100 diastolic. Her chest is normal on fluoroscopic examination.

The urine was normal except for a slight trace of albumin. The blood showed a hemoglobin content of 14.8 to 15.5 Gm., an erythrocyte count of 5,360,000 and a leukocyte count of 7,700, with a differential count of neutrophils 67 per cent, large lymphocytes 0 per cent, small lymphocytes 24 per cent, monocytes 8 per cent and eosinophils 1 per cent. The sedimentation rate was 4 mm. in half an hour and 8 mm. in one hour. The Kahn reaction of the blood on March 12, 1945, was negative.

There are firm, nontender, cutaneous and subcutaneous nodes of different size, ranging between 3 by 5 and 11 by 11 mm. in diameter, about the elbows. Four nodes are on the left arm and two on the right arm. Most of them are flesh colored; one is bluish red (embedded in a surgical scar), and one is brownish. The lesion in the right parietal area of the scalp is a fibrous cutaneous nodule 5 mm. in diameter.

The histopathologic examination of a section taken from the node on the left elbow showed perivascular infiltrate masses consisting of lymphocytes and plasma

cells. There was considerable fibrosis and in the deeper layer degeneration of fibrotic collagenous fibers. The walls of the small vessels were thickened.

DISCUSSION

DR. STEPHEN ROTHMAN: It is generally assumed that juxta-articular nodes are pathognomonic for syphilis or yaws, but in the case presented no evidence whatsoever could be found for either of these diseases.

DR. L. H. WINER, Beverly Hills, Calif.: Originally, in the first reports, it was the concept that these nodes had something to do with tropical syphilis. Subsequently the Harvard group found juxta-articular nodes associated with yaws. About two years ago Dr. Sweitzer and I collected a series of juxta-articular nodes and were able to find some in which there was a definite clinical history of syphilis. Interestingly enough, in the only patients who had a clinical history and positive Wassermann reactions of the blood, the juxta-articular nodes consisted not only of fibroblasts but also of a great number of plasma cells, while in the other forms—for instance, in rheumatic juxta-articular nodes and in the traumatic type, where the person worked in an occupation which caused repeated bruises over the articular surface—almost pure fibroblasts were present and subsequent fibrosis developed. We concluded that in these persons with juxta-articular nodes this response was an increased sensitivity of the collagen to proliferate and form a more or less protective pad against trauma. One of the other types of juxta-articular nodes we studied was that in rheumatic patients with rheumatoid arthritis. In this disease we were able to say definitely that practically always there was a central degeneration surrounded by fibroblasts in palisade configuration which produced a cyst with a pseudoretaining membrane. We definitely concluded that juxta-articular nodes were not always syphilitic in nature.

Linear Scleroderma with Spina Bifida. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. H. KRYSA.

R. H., a white boy aged 8 who was admitted to the pediatric-neurologic service of Dr. D. N. Buchanan, has a history of cutaneous lesions of three years' duration. The lesions first appeared on the right foot and ankle shortly after a vaccination for smallpox. Approximately six months later a lesion on the left side of the abdomen made its appearance, and recently a lesion on the right leg and thigh has become more noticeable. The patient had roentgen ray treatments and used different ointments, with some improvement.

At the present time there are lesions of linear scleroderma on the inner aspects of the right thigh, right leg and right foot. The right foot is definitely smaller than the left. A pigmented, nonatrophic spot is present on the left side of the upper part of the abdomen, with a sharp linear border in the midline. There is fibrosis of the muscles and tendons in the right foot.

The roentgenogram revealed the presence of spina bifida in the first to the third sacral segment. According to neurologic opinion, the distribution of the lesion in combination with spina bifida indicates a probable myelodysplasia at the ninth dorsal and first sacral levels.

The orthopedic examination revealed second degree fibrosis of the muscles and tendons in the right foot.

The laboratory findings were within normal limits, and the serologic reactions of the blood were negative.

DISCUSSION

DR. THEODORE CORNBLEET: I should like to suggest the possibility that the lesion is a linear nevus. It developed at the age of 2.

DR. STEPHEN ROTHMAN: *Sclérodermie en bandes* has in most cases a segmental distribution or follows the course of peripheral nerves. On the extremities there is a definite decrease of the total volume of the limb. The histologic specimen in this case shows typical scleroderma.

A Case for Diagnosis. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. H. D. OMENS.

G. R., a Negro woman aged 52, presents numerous brownish papules which are present on the chin and the anterior part of the cervical region. The duration of this disease is two months. The Wassermann and Kahn reactions were both negative.

The histopathologic examination revealed a hyperkeratosis and decided increase in the granular layer. There were a lymphocytic infiltration in the upper corium and a migration of lymphocytes in the basal cell layer, with the presence of liquefaction degeneration of the basal cell layer.

DISCUSSION

DR. MARCUS R. CARO: I thought that clinically this was a difficult condition to diagnose, but histologically both specimens showed changes typical of lichen planus. In one specimen the pathologic changes were around a hair follicle. That would fit in with the diagnosis of lichen planopilaris.

DR. JOHN F. MADDEN, St. Paul: I think that this case is an example of lichen planus annularis.

DR. MAURICE OPPENHEIM (by invitation): I thought in this case of vaselinoderma verrucosum. Histologically the case reminded me of cases of vaselinoderma verrucosum which I published in the *Archiv für Dermatologie und Syphilis* in 1916, during World War I, caused by the impure war petrolatum. Histologically the same changes—hyperkeratosis and cellular infiltration sharply limited to the papillary layer—were present. This patient shows a large number of comedos and a number of follicles and hyperkeratotic areas like warts which can be caused by the use of impure petrolatum.

Tuberculosis Verrucosa Cutis and Tuberculosis Colliquativa. Presented by DR. MARCUS R. CARO and (by invitation) DR. A. BUCHHOLZ and DR. H. C. SCHORR.

In J. J., a Negro man aged 30, syphilis developed in 1930, for which he received irregular treatment for one year. In 1937 the Kahn reaction of his blood was positive, and he was treated irregularly for two more years. After enlisting in the Army, he received additional antisyphilitic treatment from February 1943 to February 1944, which had no effect on his present lesions.

In 1942 a tender nodule developed in the left supraclavicular region, which disappeared after a few months. A similar nodule appeared in the midline of the neck; this was incised and produced a chronic draining sinus. A year later this was again treated surgically, and it healed. A new nodule then appeared below the chin and one at the right angle of the jaw. The former healed after a few months, while the latter is still draining. The patient was examined while in an Army hospital, but the findings are not available at present. A roentgenogram of the lungs is reported by the patient to have been negative for tuberculosis.

At the present time on the front of the neck there is a sharply outlined circinate patch 7 by 5 cm., with a bluish red, slightly raised and verrucous border and with central clearing. There are fused and matted, firm, enlarged lymph nodes under the chin and right side of the jaw, which at one point show definite fluctuation. At the right angle of the jaw there is a draining sinus.

The examination of the blood showed 4,500,000 erythrocytes and 9,600 leukocytes, with a differential count of lymphocytes 46 per cent, monocytes 2 per cent and neutrophils 52 per cent. The Kahn reaction of the blood was positive (2 plus), while the cholesterol Wassermann reaction was positive (3 plus). Tuberculin in a dilution of 1:100,000 elicited a strongly positive reaction.

A biopsy specimen from the margin of the verrucous lesion on the neck showed in one area an abscess which extended from the surface to the midportion of the corium. Elsewhere the epidermis showed irregular acanthosis. The papillary

layer was vascular, and it contained many pigment-bearing cells. In this layer and just below it were many tubercles composed of epithelioid cells and giant cells with a profuse sprinkling of lymphocytes. Acid-fast bacilli could not be demonstrated by the Ziehl-Neelsen stain.

Lupus Vulgaris with Squamous Cell Epithelioma. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. D. COHEN and DR. E. KAGEN.

B. R., a white man aged 39, has had cutaneous lesions since he was 3 years old. These lesions began on the left foot and then developed at various sites until now a large part of the cutaneous surface is involved. A squamous cell epithelioma formed on the left arm, which received an amount of roentgen rays that left an ulcer. After this, part of the arm was amputated in 1942. A cutaneous horn appeared at the stump, which was removed surgically six weeks ago. There is a broad superficial ulcer on the left side of the neck, which has been present for two years.

At present a good part of the skin is involved by squamous patches of dermatitis. These are sharply outlined and feel indurated. There are outlined nodules beyond borders of many of the plaques. There are atrophic scars present in some places, as over the right cheek. The right great toe is edematous and shows an ulcer with sharp smooth borders. The base is clean.

Scrofuloderma. Presented by DR. DAVID V. OMENS and (by invitation) DR. H. O. OMENS and DR. M. S. KAGEN.

In A. W., a Negro woman aged 55, there developed a swelling on the anterior surface of the neck one year ago, which became pointed and drained. This drainage gradually diminished, leaving a red crusted area. One month ago redness and swelling in the right posterior auricular area occurred, which opened and drained, leaving an undermined quarter-sized ulcer. The regional nodes are enlarged and firm.

The urine was normal. The roentgenogram of the chest was normal. A biopsy specimen of the skin of the neck revealed tuberculosis with small areas of caseation.

DISCUSSION OF THE THREE PRECEDING CASES

DR. H. E. MICHELSON, Minneapolis: In the first patient, the Negro man with the lymph nodes of the neck and plaque on the skin, I think that the plaque will turn out to be lupus vulgaris.

The case of the white man with the extensive involvement, more than one half of his integument being involved, is interesting because he has been able to go along for these many years and his main economy is hardly disturbed at all. He has lupus vulgaris, but of a mild type, which is not disturbing him. Certainly no treatment is now indicated unless one should try some of the newer schemes as have been suggested by Neubauer.

The last patient emphasizes the fact that has been expressed here before. It used to be thought that involvement of the lymph nodes in tuberculosis was confined largely to young people, but it is certainly found occurring often in people well along in life.

DR. STEPHEN ROTHMAN: In the patient with lupus vulgaris I should like to take exception to the statement that there is no infiltrate. The infiltrates are easily palpable.

DR. OLIVER S. ORMSBY: I want to call attention to the fact that in the white man the extent of the lupus vulgaris is much greater than is usually seen. I saw this patient twenty-one years ago, when he had just a moderate amount of lupus vulgaris on the sides of the face and neck. In these twenty-one years it has become extensive, as seen today. As a rule, lupus vulgaris remains for years limited to comparatively small areas. Sometimes the lesions will cover both sides

of the face and ears, but that is the extent of it. The same is true with patches on the body that will remain for many years without extension.

The lesion on the neck in the first patient shown I think is lupus vulgaris.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Some time ago my associates and I observed an elderly man, past 80 years, who had had a circumscribed palm-sized plaque of lupus vulgaris on the upper arm, which had been present since the age of 4.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Michelson that the first case is one of lupus verrucosus. Tuberculosis verrucosa in white persons looks different. The clinical picture could be different when seen in the Negro. Tuberculosis verrucosa or necrogenic wart has to be differentiated from lupus verrucosus. The first is an external infection by contact with the tubercle bacillus; the latter is caused by transportation of the tubercle bacillus from an internal focus into the skin.

DR. JOHN F. MADDEN, St. Paul: Lupus vulgaris may be the forerunner of other types of tuberculosis, which may lead to incapacity and even death. I have in mind a man who had lupus vulgaris for many years. During the past five years there developed tuberculosis of the right shoulder, which was followed by ankylosis of the shoulder joint, tuberculosis of one kidney, which was surgically removed, and, finally, bilateral pulmonary tuberculosis, followed by death. The response to tubercle bacilli is entirely individual.

DR. MARCUS R. CARO: In answer to Dr. Rothman, our patient had syphilis before the appearance of the verrucous lesions. Whenever a case is presented with the diagnosis of tuberculosis verrucosa cutis there is always considerable discussion, and often it is difficult to differentiate it from verrucous lupus vulgaris. In this case the diagnosis was made on histologic grounds. The findings present here of acanthosis, vascularity of the papillary layer and abscess formation are seen oftener in tuberculosis verrucosa cutis than in lupus verrucosa.

DR. THEODORE CORNBLEET: We have been watching, helplessly, the relentless progress of our patient's extensive lupus vulgaris. He now has undergone two different amputations for squamous cell epitheliomas. Dr. Michelson is, of course, right that treatment in such a case is inefficient, but we must keep trying.

DR. DAVID V. OMENS: I have nothing more to add regarding my case. I should like to say a word relative to tuberculosis and lupus vulgaris. About four or five years ago Dr. Ebert and I were fortunate to find a patient with that condition and hospitalized him. He was a man aged 55 who had disseminated lupus vulgaris which involved two extremitits and destroyed the eyes. He eventually died. We got a history of his having had the disease in childhood. It was progressive until the termination of life.

Nevus Epitheliomatocylindromatosus (?). Presented by DR. E. P. LIEBERTHAL and DR. M. L. FELSHER.

A man aged 52 was first seen at Michael Reese Hospital on March 15, 1945. At that time numerous flat, dime-sized to quarter-sized, dark red, closely grouped, firm, freely movable, nodular lesions were discernible on the forehead, extending from 2 cm. below the hair line onto the scalp for a distance of 5 inches (12 cm.). The surfaces of these closely grouped lesions revealed numerous telangiectases. Isolated subcutaneous, firm, cherry-sized lesions were also present on the scalp. The preauricular and postauricular areas also revealed firm, dark red, nodular lesions of sharp configuration. The patient maintained that he first noticed lesions at the hair line one year ago, which is questioned.

The blood chemistry and serologic and hematologic examinations failed to reveal any abnormalities.

In the past month the lesions on the forehead have cleared materially without any therapy. Because of inguinal adenopathy on the right side one of the inguinal

nodes was removed for examination. The pathologic report rendered by Dr. Otto Saphir was giant follicular hyperplasia.

DISCUSSION

DR. MARCUS R. CARO: I thought that clinically this was a case of sarcoid. Histologically, however, while there were sharply outlined nests of cells, I could find only a few epithelioid cells. I do not believe that it is a nevus. I should like to see more sections with special stains before venturing a diagnosis.

DR. L. H. WINER, Beverly Hills, Calif.: The microscopic section showed an infiltration of cells which resembled most closely reticular cells. The microscopic section of the lymph node showed that the normal structure of the lymph node was replaced by dense masses of eosinophilic staining cells, which to me were reticular cells. I am thinking clinically as well as histologically of mycosis fungoides in the case.

Psoriasis of the Palms. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. E. A. SKOLNIK.

The patient, a man aged 56, presents a papular eruption covered with silvery white scales on the posterior surface of the body, a few on the anterior surface and on the arms, forearms and legs. The lesions are most pronounced on the extensor surfaces of the arms and forearms, at the elbow and below the knees. The eruption is of four years' duration and mildly pruritic. On the palms of both hands there are dime-sized reddened patches covered with silvery white scales. The scales seem to be attached to the margin of the patches.

The Wassermann reaction of the spinal fluid was strongly positive. The patient is being treated for syphilis and has received fourteen injections of a bismuth preparation in oil intramuscularly to date. He is also taking phenobarbital. The urine was normal, and the blood cell count was within normal limits. The patient was seen for the first time yesterday afternoon.

DISCUSSION

DR. MARCUS R. CARO: In addition to all the typical lesions the patient presented, the lesions that interested me most were those on the knuckles. My associates and I have seen a number of patients with lesions on the knuckles that seemed to be neurodermatitis but later proved to be psoriasis. Some years ago we performed a biopsy on a specimen from one of these lesions on the knuckle and found it to be psoriasis histologically. Later psoriasis developed on the elbows and knees, confirming the histologic diagnosis. Whenever a patient with this type of lesion on the knuckle is seen, psoriasis is a good disease to keep in mind.

Multiple Superficial Epitheliomatosis. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. C. SCHORR.

J. D., a male laborer aged 65, shows lesions on the forehead, to the left of the chin and on the back. They began to appear eight years ago. The first one was in front of the left ear and received roentgen ray therapy. It now shows a linear scar. The second lesion appeared above the left eye. This has also received roentgen ray therapy. The lesion near the chin was curetted in another clinic. No treatment was given to the lesion on the back. There is no history of ingestion or exposure to arsenic.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I agree with the diagnosis. The question is how to treat the lesion. Large lesions of superficial epitheliomatosis that are treated with roentgen ray therapy may cause considerable difficulty later because of chronic radiodermatitis. I think that the best treatment is excision.

DR. THEODORE CORNBLEET: I agree with Dr. Reuter that operation is the best treatment for the lesions when they are seen early and are relatively small.

Facial Hemiatrophy. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. H. KRYSA.

D. H., a white boy aged 16, was first seen in the pediatric-neurologic service of Dr. D. H. Buchanan, in the University of Chicago Clinics, in April 1935, at the age of 6. He was referred from a local hospital with the diagnosis of facial hemiatrophy of the left side and a request for a dental prosthesis. At the age of 4 this boy fell from his tricycle and ran crying to his mother, who noticed an abrasion on his forehead. The following morning he had a "black eye" on the left side, and within the following six to eight weeks a difference in the size of the child's face on the two sides became apparent. His mother complained that the left side of his face was not growing.

On examination in 1935 there was atrophy of the left side of the face. The skin was shiny and atrophic below the malar bone. The mouth and nose were pulled over to the left. There was limitation of movement of the mouth and the palate on the left side. Dental roentgenograms showed the development of the two sides equally advanced, but a reexamination in 1939 showed normal development of the right side only and two teeth on the left side. Dental roentgenograms showed permanent tooth germs of both sides present but an arrest of resorption of deciduous teeth and of development of permanent teeth on the left side. Hopes for a dental prosthesis to correct the swing of the dental arch and midline of the face to the left were abandoned in 1939, when a recession of the gingiva occurred about the teeth which were scheduled for the corrective appliance.

In 1939 further progress of the hemiatrophy was obvious. A deep demarcation in the midline was noted on the forehead and chin, with the left side of the face greatly depressed. A dirty brown discoloration was evident on chin and forehead. There was an atrophy of the left lower lid and a slight lag of the superior elevator muscle as well as weakness of the left inferior oblique muscle. Compound hyperopic astigmatism on the right and left sides and red-green color blindness were found on ophthalmologic examination.

In 1945 further observations recorded the left side of the tongue as atrophied and deviating to the left, with the uvula pulled to the left and the soft palate swollen on the left side.

The skin covering the atrophic area has a sclerodermatic appearance with spotted hyperpigmentation and an extreme degree of atrophy.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: In addition to hemiatrophy I thought that I detected signs of scleroderma as well.

DR. STEPHEN ROTHMAN: The relationship of facial hemiatrophy and scleroderma has often been discussed. I agree that bandlike scleroderma and facial hemiatrophy are closely related.

Lupus Erythematosus. Presented by DR. MARCUS R. CARO.

In L. W., a white man aged 40, an eruption on the face developed in September 1942, which was diagnosed as sarcoid and was treated by six roentgen ray treatments of 75 r each and potassium arsenite by mouth for about six weeks, with no improvement. In January 1943 a sore throat developed for which he took 18 sulfadiazine tablets, followed by an almost complete disappearance of the lesions. Lesions gradually reappeared on the face, ears and arms, and they now had more the appearance of lupus erythematosus. A physical examination at this time gave normal results except for an abscessed tooth, which was removed. Roentgen ray examination of the lungs and sinuses showed no pathologic findings. A blood cell count showed a hemoglobin content of 90 per cent, 4,750,000 erythrocytes and 6,800 leukocytes, with a normal differential count. Sixteen injections of gold sodium thiosulfate were given intravenously, ranging in dose from 10 to 25 mg., without producing any change. After the last injection a high temperature developed, and the lesions disappeared for about two months.

Since that time the eruption has remained and has been treated by injections of proteolac (a nonspecific protein from milk) and by strong solution of iodine U. S. P. by mouth. Physical examination again gave normal results except for chronic prostatitis. On two occasions when sulfathiazole tablets were prescribed for the prostatitis, there was an acute exacerbation of the facial lesions after the ingestion of even 1 tablet.

At present there are on the face many pinhead-sized to pea-sized, dull red, slightly edematous, soft papules, with a few larger lesions on the sides of the jaw. Diascopic pressure shows no apple jelly nodules. There is no atrophy at the site of the lesions that have disappeared. There are whitish patches on the buccal mucosa on both sides.

A biopsy specimen taken from the right side of the jaw on Oct. 25, 1944 showed dilated and plugged follicular openings and a flattened epidermis with intracellular edema, especially in the basal layer. There were mantles of lymphocytic infiltrate about the blood vessels. The Weigert stain showed basophilic degeneration and clumping of the elastic fibers in the upper part of the corium.

Acute Disseminated Lupus Erythematosus. Presented by DR. DAVID V. OMENS and (by invitation) DR. H. OMENS and M. S. KAGEN.

In J. B., a white woman aged 27, there developed redness on both ears in September 1944. Redness of the skin on the cheeks, finger tips, eyelids, nose and forehead gradually appeared during the past six months. Arthritis of the wrist and hands appeared in February 1945. Fever and weakness occurred during the past few weeks.

The urine was normal. The blood cell count showed a hemoglobin content of 59 per cent, 3,070,000 erythrocytes and 3,450 leukocytes; the sedimentation rate was 18 mm. in sixty-three minutes.

Subacute Disseminated Lupus Erythematosus. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. C. SCHORR and M. S. KAGEN.

In S. M., an obese Negro woman aged 39, coin-sized red areas developed on the cheeks in August 1944. New lesions appeared on the extensor surfaces of the forearms within a few weeks. Shortly after, redness appeared on the ears, scalp, eyebrows and back. In November 1944 arthritis appeared in the elbow, wrist, shoulder, knee, ankle and hip joints. The involvement of the skin has remained the same for the past four months, but the patient has become weaker.

The Kahn reaction of the blood was negative, and the urine was entirely normal; 190 mm. of creatine was excreted in the twenty-four hour specimen of urine. The blood showed a hemoglobin content of 80 per cent and 7,200 leukocytes, with a differential count of neutrophils 61 per cent, eosinophils 1 per cent, lymphocytes 24 per cent and monocytes 14 per cent; the sedimentation rate was 18 mm. in forty-three minutes. The basal metabolic rate was + 9 per cent. A roentgenogram of the chest was normal. The nonprotein nitrogen was 34 mg. per hundred cubic centimeters of blood.

DISCUSSION OF THE THREE PRECEDING CASES

DR. CARL W. LAYMON, Minneapolis: A great deal of ground is being covered when these 3 cases are discussed together, and I wish to limit my remarks to the first patient shown. Facial eruptions of this type are frequently confusing from a diagnostic standpoint. Such eruptions, which are characterized by small erythematous papules over the flush areas of the face, are sometimes micropapular tuberculids. Other cases are examples of miliary sarcoid, and still others may be lupus erythematosus. In many cases an exact clinical diagnosis is impossible, and it remains difficult even after the histopathologic sections have been examined.

DR. OLIVER S. ORMSBY: I saw the first patient about a year and a half ago. The diagnosis rested between lupus erythematosus and sarcoid. I considered it to be lupus erythematosus. The infiltration was less than it usually is in sarcoid, so I agree with the diagnosis of lupus erythematosus.

DR. EDWARD A. OLIVER: What is to be done for the woman who showed the subacute disseminated type? In the ordinary discoid type ordinary measures often fail. As I looked over the proceedings of the New York Dermatological Society, I noted that Dr. Heymann, in association with Dr. Sulzberger, showed a patient with subacute disseminated lupus erythematosus who had been treated with oxophenarsine hydrochloride, with excellent results. I wonder if any one here has had experience with that drug. I have had 1 patient with chronic discoid lupus erythematosus in whom I tried administration of bismarsen, but the injections were too painful. I then tried oxophenarsine hydrochloride, giving her twelve intravenous injections, but was unable to see any improvement.

DR. L. H. WINER, Beverly Hills, Calif.: In the first patient shown, if that section were to be given to the average histologist he would diagnose it lupus erythematosus because of the lymphocytic infiltration.

The second patient reminded me and also Dr. Rothman of the condition diagnosed at the April meeting as lupus erythematosus disseminatus involving the finger tips. The sections were atypical. The patient shown today, Dr. Rothman pointed out, had lesions similar to those of his patient. In addition, this patient, as did his patient, gave a history of a rheumatic condition. I should like to ask the presenter to send us a biopsy specimen of one of those lesions on the finger.

DR. MAURICE OPPENHEIM (by invitation): In connection with therapeutic measures, I have treated subacute disseminated lupus erythematosus and lupus erythematosus discoides chronicus with acetarsone. I treated a number of patients with lupus erythematosus of the discoid chronicus type with it, some in my department at the Chicago Medical School and some in private practice, with sometimes excellent results. The first to recommend this treatment was Volk. It is such a simple treatment that I should recommend it. The method of application is the same as that used by me in pemphigus vulgaris.

DR. CLARK W. FINNERUD: In answer to Dr. Oliver's question, several years ago, at Dr. Michelson's suggestion, I used neoarsphenamine in 1 case and oxophenarsine hydrochloride in another of subacute disseminated lupus erythematosus, without any improvement. I gave it up.

In the first patient shown today, the slight erosion of the buccal mucous membrane with its surrounding dilated vessels and little white striae makes me favor the diagnosis of lupus erythematosus. At first glance, however, I thought that it must be an unusual sarcoid.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Patients with disseminated lupus erythematosus not infrequently present a false positive serologic reaction for syphilis. In the acute phases this may appear in 16 to 20 per cent of the cases. Occasionally such persons have been treated for syphilis by the routine use of arsphenamines, and almost always there results a severe reaction of intolerance and a precipitation of the terminal phase of the disease. The use of the arsphenamines should be limited to the more or less chronic discoid forms of the disease.

DR. MARCUS R. CARO: I have nothing to add on my own case.

In answer to Dr. Oliver's question concerning therapy in the subacute type, I have under my care a patient who, about a year ago, had lesions of subacute disseminated lupus erythematosus on the ears, face, scalp and forearms and extending over the body which were rapidly becoming worse. At that time I heard Dr. Cannon's paper on the use of strong solution of iodine U. S. P. in this disease. I prescribed it, and the eruption began to improve promptly and it was cleared within a few months. I saw him just yesterday, and he is still entirely well.

DR. STEPHEN ROTHMAN: In the era before the use of gold preparations I treated a number of patients with lupus erythematosus with neoarsphenamine, with good results. But, similarly to gold and bismuth preparations, arsenicals are contraindicated in case of systemic signs such as fever or leukopenia. In the subacute disseminate form administration of small doses of quinine is often beneficial. I should like to ask if anybody has had experience with quinacrine hydrochloride (atabrine).

DR. DAVID V. OMENS: I agree entirely with Dr. Brunsting's remarks. In the last six years I had at least 6 cases of lupus erythematosus in which I tried neoarsphenamine, using 0.15 Gm., which usually gave a severe reaction. My associates and I have used quinine but have not had good results with the internal administration of quinine. I should hesitate to use it in an acute case.

DR. THEODORE CORNBLEET: I think that my patient has the subacute variety rather than the chronic discoid type, simply because she has had sufficient systemic symptoms to go with the cutaneous lesions. She has had fever, and weakness developed.

A Case for Diagnosis. Presented by DR. F. E. SENEAR and (by invitation) DR. C. H. STUBENRAUCH JR.

T. V., aged 17, was seen for the first time on Oct. 23, 1943. At that time he stated that he had an eruption on his back of about eight or nine months' duration. The eruption was asymptomatic except for slight itching immediately after bathing. He had had no therapy other than occasional treatments with ultraviolet irradiation. At that time he presented a profuse eruption on the upper part of the trunk and the arms, especially on the extensor surfaces, consisting of tiny, discrete, follicular, pinpoint to pinhead-sized, skin-colored to pinkish red papules, some of them with keratotic tops. A few similar lesions were present on the face.

Vitamin A, 50,000 units a day, was prescribed, and when the patient was seen again, three months later, there was no change in the extent and appearance of the eruption.

On April 17, 1945 the patient was seen again, at which time the eruption was similar in appearance to that which was present in 1943.

DISCUSSION

DR. CLARK W. FINNERUD: I thought that it was keratosis pilaris. I think that many persons have this disease in some degree for years before they notice it. He has had it for three years. It is not remarkable that it has not responded to vitamin A therapy. It does help some patients but not all.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Grouped follicular lesions resembling lichen scrofulosorum sometimes appear over the seborrheic zones of the trunk in young persons who have fulminating acne vulgaris.

DR. JOHN F. MADDEN, St. Paul: I agree with the diagnosis offered by Dr. Finnerud and Dr. Brunsting. I wish to add to Dr. Brunsting's observations that sometimes the disease is a precursor to acne vulgaris.

Rat Mite Dermatitis. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. D. NIEDERMAN.

H. H., a white man aged 53, presented himself at the University of Chicago dermatology clini. on April 18, 1945, with a history of having had severe generalized pruritus for several months. He noticed small pruritic "blisters" on the trunk and extremities which discharged a clear fluid on scratching. The pruritus has a burning character and causes him to awaken from sleep. His only treatment before coming to this clinic was sulfathiazole ointment, which did not help the disease.

On physical examination at that time punctiform crusts were found on the back, in the inguinal folds and on the wrists and legs. These crusts were arranged in groups. In addition, there were diffuse dryness and scaling of the skin. The tentative diagnosis of dermatitis herpetiformis combined with asteatosis was made.

At his next visit, one week later, the patient presented numerous urticarial wheals of 3 to 5 mm. in diameter, all displaying hemorrhagic central puncta and present on the arms and neck. On being questioned about the possibility of infestation with bedbugs, the patient replied that he had noticed a long time ago that his

itching spells occur only at home. A few days later he telephoned, stating that the search he and his wife made for bedbugs in their apartment, situated behind a radio shop, was unsuccessful. However, he said, he found tiny, pinpoint-sized, black animals moving on his skin and biting him. He succeeded in catching two of them and pasted them on tissue paper with glycerin. On microscopic examination this animal proved to be a mite which was tentatively diagnosed by the Parasitology Department of the University of Chicago as belonging to the genus Liponyssus. On questioning, the patient confirmed the suspicion that the house is infested with rats. He stated that these are giant sewer rats and that there are large numbers of them around which have been killed by neighborhood dogs.

The laboratory examinations were noncontributory.

As far as we can establish, this is the second instance of rat mite dermatitis in Chicago. The first was reported by L. F. Weber (*J. A. M. A.* **114**:1442, 1940). Recently a review of all cases in the United States was published by C. R. Anderson (*Arch. Dermat. & Syph.* **50**:90, 1944).

DISCUSSION

DR. STEPHEN ROTHMAN: Dr. Weber was the first one to report 5 cases in Chicago. Both the attitude of the patient and that of the physician consulted was remarkable in our case. The patient was outraged when I first questioned him about bedbugs, but he did not find anything shocking when, after our microscopic diagnosis, he had to admit that there are rats in the walls of his house. The physician told him that he had ringworm deep in his skin and needed roentgen ray therapy.

Acanthosis Nigricans, Juvenile Type. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. A. L. SHAPIRO.

E. I. G., a white business executive aged 41, was referred to Albert Merritt Billings Hospital on March 12, 1945 by a psychiatrist, with the tentative diagnosis of psychogenic obesity. The patient stated that he had been underweight up to the age of 7. In the next years he became "rather plump," but later, taking part in athletics, became thin again. At the age of 18 he weighed 175 pounds (79.4 Kg.). At this time he was found to have tachycardia and was told to cease participation in athletics. From then on he gradually gained weight (5 to 10 pounds [2.3 to 4.5 Kg.] a year) until he reached his present weight of 360 pounds (163.4 Kg.). In the last two years he has gained 60 pounds (27.2 Kg.). However, he always has been able to lose weight by rigorous dieting. On admission to the hospital he complained of dyspnea, orthopnea, some swelling of the legs, insomnia and frequency of urination. According to the referring psychiatrist's information, the patient had been impotent for several years. Family history revealed obesity of the patient's mother and one maternal aunt.

On physical examination this excessively obese man was found to breathe with slight difficulty when lying in bed, but thoracic and abdominal organs were found to be normal. The external genitalia were normal. The blood pressure was 135 systolic and 80 diastolic and not essentially elevated after exercise.

On the skin numerous papillomas and cutaneous tags were seen on the eyelids and neck, in the axillas, around the navel and in the groins. Pigmented areas with papillary hypertrophy were present in both axillas and on the medial surface of the thighs.

The electrocardiogram revealed slight myocardial abnormality. The basal metabolic rate was + 1 per cent. The roentgenogram of the chest and sella were normal. The urine contained small traces of albumin but no cells. The blood showed a hemoglobin content of 16 Gm., 5,400,000 erythrocytes and 9,500 leukocytes, with a normal differential count. The total protein contents and the albumin-globulin ratio were normal. The fasting blood sugar content was 87 mg. The

dextrose tolerance test showed delayed rise and delayed fall (fasting value 73 mg. per hundred cubic centimeters, one-half hour value 105 mg., one hour value 142 mg., two hour value 152 mg. and three hour value 102 mg.).

The ophthalmologic examination revealed normal visual fields and normal fundus but slight sclerosis of the retinal vessels.

The histologic changes were typical of those in acanthosis nigricans.

DISCUSSION

There was no discussion of this case.

Lymphoblastoma. Presented by DR. FRANCIS E. SENEAR, DR. MARCUS R. CARO and (by invitation) DR. P. K. WEICHSELBAUM.

In J. W., a white man aged 59, asthma developed in 1939, since which time he has lost 62 pounds (28 Kg.) in weight, 14 pounds (6.4 Kg.) during the past two weeks. About two years ago there first developed an itchy eruption on his back. This spread gradually, the scalp becoming involved about four months ago. Recently there has been a progressive loss of strength as well as of weight.

The patient entered the hospital on May 10. The physical examination showed bronchial asthma, a generalized lymphadenopathy, an enlarged liver and the cutaneous eruption. The examination of the blood showed a hemoglobin content of 11 Gm., 3,550,000 erythrocytes and 12,500 leukocytes, with a differential count of stab forms 12 per cent, neutrophils 52 per cent, eosinophils 22 per cent, basophils 1 per cent, lymphocytes 10 per cent and monocytes 3 per cent. The Kahn test of the blood gave a negative reaction. The urine contained albumin (3 plus). Aspiration of the sternal marrow showed some myeloid immaturity with increased numbers of eosinophils. It was the hematologist's impression that this was a case of lymphoblastoma (Hodgkin's disease or mycosis fungoides) and not leukemia or lymphosarcoma. Since the patient entered the hospital, his temperature has ranged from 96.2 to 101.4 F. by mouth.

The eruption is generalized, the only parts spared being the palms, soles and genitalia. There are many large, soft, purplish red nodules on the dorsal surface of the feet and on the legs, thighs and buttocks, with considerable brownish pigmentation. On the back of the hands and on the forearms and arms the nodules are also large but are less profuse. There are large ulcerated nodules over the right eyebrow and on the lobe of the left ear, and many of the other large nodules are ulcerated and crusted. There are also many smaller papules on the face, scalp and trunk and many scars, especially on the back. On the trunk and forearms there is a diffuse eruption of closely set, pinhead-sized, round, brownish papules that gives the skin a cobblestone-like surface.

A biopsy performed on a nodule from the arm showed a slight acanthosis of the epidermis, a dilatation of the blood vessels and lymphatic vessels in the upper part of the corium and a densely packed cellular mass involving nearly the entire corium. In this cellular infiltrate there was a multiplicity of cells, including many eosinophils and a few multinucleated cells suggesting the Sternberg-Reed cell. A biopsy specimen from a small papule on the chest showed, on histopathologic examination, a small, circumscribed mass of cellular infiltrate just below the papillary layer of the corium. The cell types were the same as those in the larger lesion, but there were, in addition, many chromatophores lying below the basal layer.

DISCUSSION

DR. MARCUS R. CARO: I want to apologize for presenting this as a case of lymphoblastoma without a more specific description as to type. The patient came in last Thursday, and a biopsy was performed but the studies have not been completed.

NOTE.—Histologic examination of a lymph node from the left axilla showed the changes of a Hodgkin type of lymphoblastoma.

Calcinosis, Generalized. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. Z. FELSHER.

G. M., a white woman aged 66, was first admitted to the Albert Merritt Billings Hospital in 1934 with a history of generalized calcinosis of ten years' duration. On admission she complained of swelling of the ankles, heaviness of the limbs and calcareous plaques in the subcutaneous and muscular tissues of both groins, buttocks, abdominal wall and extremities. She had had a series of discharging abscesses of calcareous material and pus. These have varied from pinpoint size to 8 by 4 cm. During the past few years there have been no more recurrent sinuses. Primarily all lesions were located in the subcutaneous fat, but secondarily they involved the corium.

The physical examination reveals a poorly nourished 66 year old woman who is a semi-invalid. The left elbow cannot be extended beyond 50 degrees, and there is also some limitation of extension of the right knee. There is limited flexion, extension and side bending of the neck. The knees cannot be flexed beyond 50 degrees, and the thighs cannot be flexed more than 45 degrees. All motions of the ankles are limited. Large, hard plaques are found throughout the subcutaneous and cutaneous tissue, most evident in the medial aspect of the left arm, lower part of the left side of the abdomen, suprapubic area, both groins, medial and lateral aspects of the thighs, perineum and over the hamstring muscles and legs.

The urine was normal, as were the blood cell counts and differential counts. The Kahn reaction was negative. Nonprotein nitrogen, urea nitrogen and plasma protein contents were within normal limits. The albumin-globulin ratio was 1.75. The serum calcium level was 9.1 mg. and the serum phosphorus content 4.39 mg. per hundred cubic centimeters; the serum phosphatase level was 5 units per hundred cubic centimeters, which is normal. The tests of renal function showed no abnormality.

The roentgenologic examination revealed many areas of calcification in the subcutaneous tissue.

The histologic examination of a biopsy specimen of fibrous tissue attached to a surgically removed bunion showed areas of calcification.

DISCUSSION

DR. THEODORE CORNBLEET: In this patient, as in many similar ones, the blood calcium and protein levels remain within the normal range of values. In some, even subnormal values for calcium are found. The explanation for the deposits in the skin would not seem, therefore, to be the simple one of an excess spilling out of the blood. In most patients the onset may be associated with some systemic or toxic process. In the case of this patient, she dates her trouble definitely to the time when she had a severe sore throat which lasted for a while.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Deposits of calcium occurring in the skin, especially about the joints, develop in the terminal and chronic stages of dermatomyositis, but in this case there seems to have been no history of such a disorder.

DR. STEPHEN ROTHMAN: I agree with Dr. Cornbleet that this is a primary generalized calcinosis. There is no evidence either in the history or in the clinical findings which would suggest that the deposits of calcium have been secondary to some inflammatory process. I wonder whether such calcinosis ever has been reported subsequent to dermatomyositis.

Pityriasis Rubra Pilaris with Exfoliation. Presented by DR. THEODORE CORNBLEET, DR. MICHAEL EBERT and (by invitation) DR. M. S. KAGEN.

J. B., a Negro aged 45, presented a generalized hyperkeratosis when seen six months ago. The palms and soles were greatly thickened and had several fissures. The skin on the legs had become greatly thickened, being verrucous in nature. In March 1943 the skin became rough and gradually increased in thickness and

pigmentation. In January 1944 the disease had reached a standstill, vitamin A being of little help.

The patient reentered the Cook County Hospital on May 9, 1945, complaining of cough, dyspnea and weakness. The face was flushed, the alae nasi were dilated and dulness over the lower lobe of the left lung revealed pneumonia. The liver was enlarged to five fingerbreadths beneath the right costal margin. Both fever and dehydration were believed to have played a role in producing exfoliation on the chest, back, arms and thighs.

The urine was normal. The Kahn reaction of the blood was negative. The blood showed a hemoglobin content of 78 per cent and 14,000 leukocytes. The vitamin A and carotene levels were normal.

DISCUSSION

DR. THEODORE CORNBLEET: The reason I felt that it was worth while presenting this patient was that there was such an extensive exfoliation on parts of the body. Where that had taken place, the skin beneath seemed normal but slightly red. Since last week some of these exfoliative areas have been occurring in the regular form of pityriasis rubra pilaris. I felt that it might point up a method for treatment of this resistant syndrome.

NOTE.—Since penicillin was used in treating the patient's pneumonia, it was tried for its effect against the cutaneous process itself, which returned shortly. This was without benefit, as was the administration of enormous doses of vitamin A over an extended period. It was felt, therefore, that the temporary improvement resulted from the fever while the lobar pneumonia developed.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. THEODORE CORNBLEET and (by invitation) DR. M. S. KAGEN.

J. W., a Negro man aged 61, had his prostate resected at the Cook County Hospital three years ago. Three weeks later redness of the skin appeared on the face, neck, dorsa of the hands and forearms. This disappeared in a few weeks, recurring several times during the next two years. During the past year redness persisted on the neck, face, flexor surfaces of the knees and elbows. Three weeks ago the dermatitis on the previous areas became severer and extended to the entire body except the palms, soles and back. The patient has become nervous and weak and complains of severe itching.

The urine was normal. The roentgenogram of the chest was normal. The blood chemistry showed a nonprotein nitrogen content of 30 mg. and sodium content of 134 mg. per hundred cubic centimeters. The blood showed 4,200,000 erythrocytes and 5,700 leukocytes, with a differential count of neutrophil polymorphonuclears 72 per cent, lymphocytes 24 per cent and monocytes 2 per cent.

The histologic examination of a biopsy specimen of an inguinal node revealed a nonspecific lymphadenitis. There was a decided increase in the number of eosinophils, and a large amount of blood pigment was also seen.

DISCUSSION

DR. L. H. WINER, Beverly Hills, Calif.: I wish to comment on the splendid imprints that the presenter showed. Though they were normal, the technic of staining was important and they were fine. One will observe the fine reticular cells where there is definite reticular hyperplasia.

A Case for Diagnosis (Pemphigus?). Presented by DR. MICHAEL EBERT and (by invitation) DR. M. S. KAGEN.

V. T., a white man born in Italy and aged 41, presents an itching and burning eruption which has been fairly generalized. He stated that this began two years ago with a swelling of the glands of the neck associated with some disturbance of the nose and throat. Shortly after, a crop of blisters appeared in the axilla and spread from there. He has been hoarse for several months and complains of nasal

obstruction for the same period. He has been treated by a private physician for the past year. He reports exacerbations and partial remissions of the eruption.

When admitted to the hospital two weeks ago this man had numerous bullae and edematous maculopapules. At present the eruption is much less evident. The lesions are most numerous on the extremities, neck and chest. There are a few small bullae with an areola of erythema, several crusted erosions and bluish red maculopapules with many discolored relics. Nikolsky's sign can be elicited. He has one small erosion on the buccal mucosa. The department of otolaryngology reports that the vocal cords are thickened and covered with an adherent secretion and that there is decided crusting of the nasal cavities.

The blood showed a hemoglobin content of 78 per cent and 6,500 leukocytes, with a differential count of neutrophils 57 per cent, eosinophils 2 per cent, lymphocytes 36 per cent and monocytes 5 per cent.

The patient is in good physical condition. He has taken 0.5 Gm. of sulfapyridine four times a day for two weeks, and his condition has improved.

DISCUSSION

DR. CLEVELAND J. WHITE: I saw this man last fall, at which time he presented noninflammatory bullae of the mouth. Some of the lesions were slow in healing, and the mouth was painful. He had a few flaccid bullae on the shoulders. The phytotoxic test was performed at that time, and a diagnosis of pemphigus was suggested. Various kinds of treatment were used. Today he presents bizarre, purplish lesions, especially on the trunk, suggesting that the case might belong with the lymphoblastoma group. At the time I saw him it was definitely pemphigus in my opinion.

MINNESOTA DERMATOLOGICAL SOCIETY

S. E. Sweitzer, M.D., *President*

H. A. Cumming, M.D., *Secretary*

May 18, 1945

Alopecia Areata in an Infant. Presented by DR. S. E. SWEITZER, Minneapolis.

S. M., a Negro infant aged 6 months, began losing her hair two months ago. Her previous health was good; she was a full term baby. Serologic reactions for syphilis were negative.

Examination reveals a patchy loss of hair throughout the entire scalp. In many areas regrowth has begun.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: My associates and I could not find anything with the Wood light and on culture. I have never seen such a young child with alopecia areata.

Lupus Erythematosus of the Scalp. Presented by DR. S. E. SWEITZER, Minneapolis.

H. H., a man aged 60, stated that for the past year he has had an eruption on the scalp.

Examination reveals three or four areas ½ to 1 inch (1.2 to 2.5 cm.) in diameter on the top of the head devoid of hair. The skin in these areas is atrophic and red. A papular eruption is present over the forehead, nose and malar areas of the cheeks. Histologic sections were shown.

DISCUSSION

DR. L. H. WINER, Minneapolis: There are different types of lupus erythematosus. The feature that stands out most here is the presence of hair follicles

without hair. The essential observation that one can rely on in a microscopic diagnosis of lupus erythematosus is the degeneration of connective tissue, perifollicular islands of infiltration and loss of hair. There is no other disease, I think, that gives the lymphocytic round cell infiltration of this type and loss of hair with it.

Dr. John F. Madden, St. Paul: I do not think that this eruption is lupus erythematosus. There are none of the characteristics of that disease. It seems more like a pyogenic infection which has resulted in scarring.

Dr. S. E. Sweitzer, Minneapolis: If one thinks it over, there are three disorders which this could resemble in the scalp: lupus erythematosus, folliculitis decalvans and pseudopelade of Brocq; it does not look like folliculitis. I do not think that it is pseudopelade, so I am inclined to believe that it is lupus erythematosus on the scalp. These conditions are difficult to diagnose.

Acanthosis Nigricans (Juvenile Type). Presented by Dr. Carl Laymon, Minneapolis.

L. S., a woman aged 22, has noticed darkening of the skin over the body folds since she was in grade school. Her general health has always been excellent. Examination reveals light brown, slightly verrucous plaques in the axillas and groins, around the neck and under the breasts.

DISCUSSION

Dr. Louis Brunsting, Rochester, Minn.: This is a classic example of juvenile acanthosis nigricans showing the characteristic hyperpigmented verrucous changes in the skin on the neck, groin and axillas. There seemed to be no contributing causes from the general standpoint.

In most instances of the adult type of acanthosis nigricans there is evidence of abdominal malignant growth sooner or later. I can recall three instances in which exploration was done, with normal results at the time of operation. However, 2 of the patients died within a period of six months from fulminating metastatic adenocarcinomatosis; the other survived for a period of more than ten years, and the cutaneous symptoms subsided. A detailed general examination is always indicated, for I believe that it is impossible to distinguish the malignant from the so-called benign types by clinical inspection.

Dr. Carl Laymon, Minneapolis: Most observers who have reported series of cases of the adult type of acanthosis nigricans have noted the association with internal malignant growth in over 50 per cent of the cases. One cannot go so far as to say that the adult type is associated with malignant growth in all cases. The vast majority of patients with juvenile acanthosis nigricans are in good health, and it is impossible to demonstrate glandular dysfunctions which could account for disturbances in the chromaffin system.

A Case for Diagnosis (Gumma of the Testicle?). Presented by Dr. S. E. Sweitzer, Minneapolis.

G. N., a man aged 60, first noted a swelling on the scrotum about four weeks ago. This spontaneously opened and discharged a yellowish fluid. The patient had gonorrhea forty-eight years ago and syphilis, which was not treated, forty-four years ago. Serologic reactions for syphilis were positive. The tuberculin test with tuberculin in a dilution of 1:1,000 was questionable. Roentgen ray examination of the chest revealed several calcifications in the right hilus.

Examination reveals a sharply punched-out ulcer, 1.5 cm. in diameter, on the right side of the scrotum. The testicle is not enlarged, and the epididymis is palpable. Since the patient received 2,400,000 units of penicillin, the pustular discharge has decreased considerably in amount. There is a cord type of bladder, with incontinence of urine. The deep reflexes are absent. The Romberg sign is positive.

DISCUSSION

DR. FRANCIS LYNCH, St. Paul: In this case the infection appears to be in the epididymis rather than in the testicle. Could it not be a pyogenic infection complicating chronic cystitis or prostatis? The response of treatment cannot, therefore, be an indication as to whether the infection is syphilitic or pyogenic.

DR. S. E. SWEITZER, Minneapolis: Well, he had a good deal of purulent discharge, so my associates and I thought that we would use penicillin. He was an old known syphilitic person. The testicle could possibly be taken out.

DR. L. H. WINER, Minneapolis: It is either syphilitic or tuberculous epididymitis. Autopsies on patients with tuberculous epididymitis showed that 90 per cent of them had tuberculous prostatitis, in the majority of which diagnoses were missed clinically, since the prostate was normal to palpation.

DR. S. E. SWEITZER, Minneapolis: Syphilis of the epididymis is rare, and, if it occurs in this location, it usually involves the testicle.

Gumma of the Nose and the Upper Lip. Presented by DR. S. E. SWEITZER, Minneapolis.

R. W., a woman aged 58, had a chancre twenty-eight years ago, for which she received no treatment. Four or five years ago her nose began sinking into her face. There was no antisyphilitic treatment until February 1945, when she was given potassium iodide. She has since received eight injections of a bismuth preparation and three of neoarsphenamine. Serologic reactions for syphilis were positive; the result of a quantitative Kahn test was 800 units. Examination reveals a nose which is almost entirely sunken into the face. There is a perforation at the hard palate, and the uvula is absent. The upper lip is slightly thickened, and an ulcer of the upper lip is rapidly healing.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: This is an old textbook picture of syphilis. It really is not seen much any more.

Cavernous Hemangioma of the Lip. Presented by DR. S. E. SWEITZER, Minneapolis.

C. K., a girl aged 1 year, has had a tumorous swelling of the lower lip since birth. Examination shows that the right half of the lower lip is enlarged with a soft, red tumor which involves the entire margin of the lip and extends downward to the gums.

DISCUSSION

DR. FRANCIS LYNCH, St. Paul: It can hardly be doubted that some hemangiomas regress spontaneously, but there is doubt as to the frequency with which this occurs. Most discussion is based on impressions rather than on factual data, with the exception of Lister's publications, indicating that spontaneous regression is the rule. It is my impression that most, though not all, cavernous hemangiomas will disappear even though not treated.

DR. H. E. MICHELSON, Minneapolis: What about mucous membrane of the lip?

DR. FRANCIS LYNCH, St. Paul: I have observed regression of lesions of the mucous membrane just as of those on the skin.

DR. L. H. WINER, Minneapolis: I think that the injection is the least harmful type of treatment. A great many of the patients are treated with injections that cause so little effect that the lesions heal spontaneously. But I think that something should be done.

DR. JOHN F. MADDEN, St. Paul: The injection of sclerosing solutions in the treatment of cavernous hemangiomas is technically difficult. This type of treatment has been unsuccessful in my hands and in cases in which I have seen injection

attempted by my colleagues. It is true that some cavernous hemangiomas disappear spontaneously, but some do not. There is no way of telling which will disappear. It would take great courage and implicit faith in your convictions to tell the parents of a child with a rapidly growing hemangioma that nothing should be done and that the lesion would disappear. It would also require a degree of faith in the doctor which the average patient does not have.

DR. S. E. SWEITZER, Minneapolis: Have you ever watched any of them grow? You mention getting a slough from injection, but if that occurs it is just the same as that which nature does a lot of times. The blood supply is cut off in the center, and the lesions fibrose in. I watched 1 patient, a boy with a large angioma on the thigh. The father refused treatment, and in the course of several years I saw this patient again. Nature had healed the lesion, and a large depressed scar resulted. The question in these cases is whether treatment will give a better-looking result than nature. I think that I get better results by treating them easy and stopping the growth, thereby obtaining a smaller and better-looking scar.

DR. FRANCIS LYNCH, St. Paul: As Dr. Sweitzer indicated, when hemangiomas are left untreated the end result is not always satisfactory. There is one group of persistent lesions which should not be regarded as hemangiomas; an example was observed at the university clinic this week, when large tortuous vessels were noted which are usually present in arteriovenous aneurysmal lesions. Some hemangiomas merely persist; others enlarge and then remain unchanged, and still others undergo the loss of substance described by Dr. Sweitzer. Superficial ulceration evidently results from too rapid thrombosis, sometimes after injury or external infections. It has been my unfortunate experience to observe such a change in treated lesions as well as in untreated ones and with comparative frequency. Even the most skilled advocates of early treatment cannot claim perfect results in all cases, and with the best results there is likely to be a depression or a superficial scar or atrophy. I believe that the best results occur when spontaneous regression is allowed (this may occur with or in spite of irradiation therapy in amounts which do no harm).

DR. S. E. SWEITZER, Minneapolis: They do not respond to irradiation therapy; cautery is much better.

Cutis Verticis Gyrata. Presented by DR. CARL LAYMON, Minneapolis.

Mrs. R. L., a woman aged 26, stated that an abnormality had been present on her scalp since birth. On examination there is a large, soft, folded, gyrate nevus on the posterior part of the scalp.

DISCUSSION

DR. JOHN F. MADDEN, St. Paul: I showed a boy 8 years of age before this society in 1934 who had the nevus type of cutis verticis gyrata. One portion of the lesion had ulcerated. Biopsies were made and the sections shown to pathologists at the University of Minnesota and the Mayo Clinic.

All made a diagnosis of malignant melanoma. The boy is in perfect health eleven years later.

DR. L. H. WINER, Minneapolis: How many years ago?

DR. JOHN F. MADDEN, St. Paul: It was in 1934.

DR. CARL LAYMON, Minneapolis: This term has been loosely applied to a number of diseases, but, in the opinion of most observers, it should be reserved for a nevoid condition, as this case exemplifies. The same term is improperly applied to certain malignant growths of the scalp as well as myxedema and deep dissecting pyodermas which result in folding of the skin of the scalp.

DR. L. H. WINER, Minneapolis: I should like to know what is thought of this lesion. Does it belong to the moles, or is it a form of von Recklinghausen's disease that is seen occasionally? Should it be let alone, or should it be removed?

DR. CARL LAYMON, Minneapolis: I did obtain permission to perform a biopsy. Some of these lesions have been ordinary common hairy moles; others have been fibromas. If the teachings of Traub are accepted, most of the hairy moles are relatively benign and I think that the danger of malignant melanoma in this case is not great.

Tinea Capitis Due to Microsporon Audouini (Three Cases). Presented by DR. S. E. SWEITZER, Minneapolis.

O. P., a Negro boy aged 8, has had a patchy loss of hair for several months. A 5 year old brother has the same disease. Fluorescence under Wood's light gave the typical green color of the microsporums. Culture revealed typical Microsporon audouini. Examination reveals numerous patches of loss of hair, with broken-off hairs and scaliness.

L. G., a Negro boy aged 6, has had a patchy loss of hair for two months. Fluorescence was typical for microsporums. Culture yielded typical growth of M. audouini. Epilation with roentgen rays was done on April 12, 1945, and the few remaining hairs were epilated with a proprietary wax on May 17, 1945. Examination reveals a scalp devoid of hair, with a diffuse thin scaliness. Fluorescence is now absent.

In D. M., a boy aged 10, a patch of alopecia developed in September 1944. Local applications were used for six months, and then on March 13, 1945 roentgen ray epilation was performed. This has been followed by local applications of ammoniated mercury and Dennie's ointment (containing 0.1 Gm. of cinnabar [mercuric sulfide], 1 Gm. of precipitated sulfur, 1 Gm. of salicylic acid, 2 Gm. of benzoic acid and 30 Gm. of petrolatum) and painting with iodine. Fluorescence and culture were typical for M. audouini. Examination reveals a beginning regrowth of hair. Fluorescence is now absent.

DISCUSSION

DR. FRANCIS LYNCH, St. Paul: The Minnesota Department of Health has recently changed its regulations so that ringworm of the scalp is again a reportable disease. Cases in the larger cities are to be reported to the local health authorities. I have just reported 2 cases to the Minnesota Department of Health, and they have taken steps to give some training to a member of their staff so that he may investigate the community in which these patients reside.

DR. S. E. SWEITZER, Minneapolis: I think that they could be treated in town. I think that they are treated here at the Minneapolis General Hospital when they live out of the city.

DR. CARL LAYMON, Minneapolis: About two months ago Dr. Lynch and Dr. Michelson and I were discussing the reasons for the increased incidence of epidermic ringworm of the scalp. It seems to me that the shifting of population in the last five years is an important factor.

DR. JOHN F. MADDEN, St. Paul: I want to bring up another point regarding ringworm of the scalp and roentgen ray therapy. General practitioners were told that roentgen ray therapy was the only means of curing this disease. Some of them are using fractional doses of roentgen rays on the infected scalp. This delays the use of or makes epilation by roentgen rays impossible at least for some time.

Dermatitis Medicamentosa Due to Gold Sodium Thiosulfate. Presented by DR. S. E. SWEITZER, Minneapolis.

E. J., a woman aged 73, has had an itching eruption of the skin for four months. For several months prior to the onset, she had been receiving injections of gold sodium thiosulfate for arthritis. Examination reveals a dry, scaling dermatitis scattered over the entire body. It is most striking on the face, neck, forearms and legs.

DISCUSSION

DR. LOUIS BRUNSTING, Rochester: There is nothing distinctive about this nummular eczematoid reaction which would make one consider it to be a reaction to gold salts.

DR. S. E. SWEITZER, Minneapolis: My associates and I have had many patients like this girl.

Atrophoderma Hypoestrogenicum. Presented by DR. S. E. SWEITZER and DR. L. H. WINER, Minneapolis.

M. T., a white woman aged 30, was shown at the Feb. 9, 1945 meeting of the Minnesota Dermatological Society. Red plaques had been present on the extremities since the age of 11. In October 1944 administration of large doses of diethylstilbesterol was begun, and the plaques disappeared. For the past two months she has been taking no medicament, and her skin remains completely normal.

DISCUSSION

There was no discussion of this case.

A Case for Diagnosis (Purpuric Eruption of the Lower Extremities Resembling Schamberg's Disease). Presented by DR. S. E. SWEITZER, Minneapolis.

G. C., a man aged 79, has had an eruption on the lower extremities for four weeks. Serologic reactions for syphilis were negative. Blood and urine were normal. Examination reveals punctate, brownish macules arranged in groups over the lower extremities, extending to and slightly above the knee. Toward the ankle there are dull red plaques covered with a thin varnish-like scale.

DISCUSSION

DR. CARL LAYMON, Minneapolis: One thing I want to say is that the more patients we see with these diseases, the less expert we seem to become, but there is one thing that strikes me and that is that most of these conditions seem to be forms of stasis dermatitis. Most of the patients that have been presented at our meetings have had varicose veins. In some instances the lesions are macular with small hemorrhagic puncta, whereas others are more papular and lichenoid, so that it depends on the clinical appearance as to whether a case is labeled Schamberg's disease or pigmented purpuric lichenoid dermatitis.

There are some features of these diseases which are not answered by stasis alone. For example, Schamberg's first patient was a boy who had lesions on the upper extremities and on the trunk. In some patients there may be an unknown toxic process which produces the same sort of lesion on areas other than the lower extremities by its effect on the blood vessels.

DR. L. H. WINER, Minneapolis: At the University of Minnesota there was a man with involvement of the skin of the lower extremities as well as of one forearm, from which microscopic sections were made and stained for iron. The tissue was loaded with iron. My colleagues and I observed histologically great numbers of capillaries and called it capillaritis. This condition was closer to Schamberg's disease than that in the case shown today. The case shown today is in my mind one of a form of purpura.

Melanosis of Riehl. Presented by DR. H. E. MICHELSON, Minneapolis.

E. V., a man aged 30 who operated a turret lathe, stated that six weeks ago he first noted dark spots appearing under his eyes and on the forehead. This has gradually increased in intensity, and about four weeks ago an eruption began on the back of his hands. He came in contact with a "soluble oil" used in cooling the metal.

Examination reveals a dry, scaly dermatitis on the forehead, around the eyes and in front of the ears. The entire skin of the face is unevenly pigmented and presents a dirty appearance. The upper portion of the forehead is normal, as is also the neck. The dorsa of the hands are rough and present a papular eruption about each follicle. No comedos or pustules are present, and the nonhairy portions of the hands are normal. This follicular eruption extends upward on the arms and gradually fades, disappearing completely at the elbow.

DISCUSSION

There was no discussion of this case.

Lichen Sclerosus et Atrophicus. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. F. M., aged 50, stated that a white streak began to appear on the right side of the neck about January 1944. This has increased in size until it is now about 4 inches (10 cm.) long and ½ inch (1.2 cm.) wide. The involved skin appears atrophic and is stippled. The lesion is asymptomatic. There is no eruption elsewhere.

DISCUSSION

DR. CARL LAYMON, Minneapolis: I agree with the diagnosis. One interesting feature in this case is the presence of the lesions in the mouth. The question usually arises whether or not this disease is a form of atrophic lichen planus. Possibly if a biopsy of a specimen from lesions in the mouth were performed, it would be found that the histopathologic findings are the same as those on the skin, and the findings here were certainly consistent with the diagnosis of lichen sclerosus et atrophicus.

DR. L. H. WINER, Minneapolis: The thing of interest histologically in this patient's section was that the upper portion of the cutis was homogenized, consistent with a diagnosis of lichen sclerosus. But beneath the cellular infiltration, the connective tissue fibers had enlarged and formed large bundles, just as one sees in scleroderma. I have never seen exactly that picture, and I call it to your attention.

Lupus Vulgaris. Presented by DR. JOHN F. MADDEN, St. Paul.

E. A., a white man aged 48, stated that what was thought to be a furuncle appeared on his buttocks in 1914. At that time the patient lived in Montana and rode horses a great deal. He thought that the original lesion appeared following an especially long period of steady riding. The abscess was incised and pus evacuated, but the lesion did not heal. A verrucous, scarring eruption spread from this area until it now involves the entire buttocks and extends up to the first lumbar vertebra and down to the midportion of the upper third of the thighs. The eruption now has a verrucous, inflammatory border with various-sized verrucous nodules studding the scarred central portion of the eruption. Some of the verrucous nodules exude pus, some are crusted and some are dry.

The patient stated that he had many abscesses in the anterior part of the cervical region on both sides of the neck about 1905. The anterior part of the cervical region on both sides of the neck is now covered with many scars. About 1912 the patient fell from a horse and broke the proximal portion of the right femur. An abscess formed and was drained. There is a scar about 4 inches (10 cm.) long on the lateral portion of the right thigh opposite the proximal portion of the femur.

Roentgenograms of the lungs were normal. The skin at the site of the Mantoux test showed no sign of erythema, but there was a slight induration at the end of forty-eight hours.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: Dr. Madden's diagnosis was lupus vulgaris. I understand that a biopsy specimen was shown at the University of Minnesota Hospital.

DR. JOHN F. MADDEN, St. Paul: It is remarkable how rapidly the eruption changes. At times it becomes purulent and angry.

METROPOLITAN DERMATOLOGICAL SOCIETY

Royal M. Montgomery, *President*

J. Lowry Miller, *Secretary*

May 21, 1945

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by DR. RICHARD J. KELLY.

S. W., a man, has had an eruption over the shoulders posteriorly, on the flexor and extensor surfaces of all extremities and about the girdle area since approximately eight to twelve weeks previous to April 19, 1945. The patient presents numerous vivid red papules in these areas, with some scaling and much vesiculation. He states that there is intolerable itching.

The patient was given fractional roentgen ray therapy, 100 r, to all areas and ointments locally.

DISCUSSION

DR. JOSEPH C. AMERSBACH: I think that the diagnosis has to be differentiated between dermatitis venenata and dermatitis herpetiformis. The eruption in this case is interesting when its distribution is considered, which I am sure was the reason for Dr. Kelly's presentation of this case. However, I wish to make a diagnosis of dermatitis herpetiformis.

DR. LESLIE P. BARKER: I believe that this is a case of dermatitis herpetiformis. The eruption is limited to the extensor surface of the arms, the shoulders, the lower part of the back and the buttocks. There are some lesions, however, in the pubic area. The eruption consists of grouped vesicles, urticarial lesions and scratch marks.

DR. ROYAL M. MONTGOMERY: I favor the diagnosis of dermatitis herpetiformis. Although some areas are sharply limited, there are typical groups of vesicles which have not been scratched. This grouping is typical of dermatitis herpetiformis. The patient should be given sulfapyridine therapy. This treatment would not help if the case were one of dermatitis venenata.

DR. RICHARD J. KELLY: I am interested in the comments because I favor the diagnosis of dermatitis herpetiformis in spite of the fact that the patient comes in contact frequently with oil in his work and also because the areas affected are those which would be in contact with oil in his clothes. There is grouping of the lesions.

Syphilis, Early Tertiary. Presented by DR. LESLIE P. BARKER.

N. D., a man aged 51, appeared at St. Luke's Hospital Clinic because of an eruption on the face. There were no subjective symptoms locally or generally. The patient has been well. The patient stated that the present eruption has recurred three times during the past eighteen months. The present outbreak developed one month ago, the day following an intravenous injection for syphilis. The doctor told him that the material being injected was penicillin, although the patient said that it was extremely dark in color. The eruption reached its full development within a few days and has remained stationary since that time.

Over the face there are about ten lesions, ranging in size from that of a large pea to that of a silver half-dollar. The lesions are firm, slightly raised and dark red. Some show a slight amount of crusting, others are scaly and one of the larger lesions on the left cheek shows some atrophy in the center. The patient had applied iodine, and one or two of the lesions show considerable irritation.

The Wassermann reaction was positive (4 plus) in a 1 to 64 dilution; Kahn and Mazzini reactions were strongly positive.

DISCUSSION

DR. RICHARD J. KELLY: I believe that this is a case of late secondary syphilis.

DR. ROYAL M. MONTGOMERY: I think that the only way to differentiate in this case between syphilis and lupus erythematosus is by a biopsy. The case suggests lupus erythematosus, but I should prefer to await the result of the biopsy for a diagnosis.

DR. JOSEPH C. AMERSBACH: This case impressed me as being one of lupus erythematosus, particularly so because of the appearance of the lesions of the ear and left cheek. It will be interesting to await the report of the pathologist in this case.

DR. J. LOWRY MILLER: I favor the diagnosis of tertiary syphilis although lesions are scattered on both sides of the face. There is definite scarring and infiltration in the lesions, and I think that this is early tertiary syphilis probably bridging the gap between late secondary and early tertiary lesions. The lesions of the ear resemble lupus erythematosus, but there is too much infiltration in many of the lesions for that disease.

DR. LESLIE P. BARKER: I think that this man gives an interesting history if it can be relied on. He stated that this is the third outbreak of the eruption in the past eighteen months and that the present outbreak followed an intravenous injection by a private physician for syphilis. The physician told him that the material being injected was penicillin, although he said that the color of the material was dark, like iodine. All the lesions show considerable infiltration, and there is some scarring in the center of the lesion on the left cheek and the ear. These are the two lesions that resemble lupus erythematosus. I think that there is no doubt that the eruption is syphilitic, either a late secondary or an early tertiary type.

A Case for Diagnosis (Granuloma Annulare? Sarcoid? Psoriasis?). Presented by DR. JOSEPH C. AMERSBACH.

I. G., aged 13, has raised, infiltrated and scaling lesions scattered over the scalp, elbows, back and buttocks, of one and a half years' duration.

DISCUSSION

DR. ROYAL M. MONTGOMERY: I think that it is an atypical lupus erythematosus, because most of the lesions are on the body. There is one in the scalp which is crusted and fairly typical of lupus erythematosus. The one on the upper part of the right buttock is atrophic in the center.

DR. LESLIE P. BARKER: This eruption is most unusual, but I believe that it is tuberculosis of the skin. One lesion on the back has a nodular border and resembles granuloma annulare. The others are definitely raised granulomas that are brighter red, however, than is commonly seen in tuberculosis and do not show the typical apple jelly nodules. Sarcoid of Boeck, however, must also be considered.

DR. RICHARD J. KELLY: I agree with Dr. Barker that the lesion over the right buttock looks similar to granuloma annulare, but I think that the lesion from which a biopsy specimen has been taken, on the upper part of the right thoracic area posteriorly, has certain features of chloasma.

DR. J. LOWRY MILLER: I favor the diagnosis of tuberculosis. I do not think that it is lupus erythematosus, because the lesions of the scalp show no loss of hair and no definite atrophy. There is definite atrophy in the lesion on the back and on the right elbow. I think that these lesions are some form of tuberculosis; exactly which type I am not certain.

A Case for Diagnosis (Squamous Cell Epithelioma?). Presented by DR. ROYAL M. MONTGOMERY.

T. D., a man aged 41 years, born in Scotland, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in April 1944. He has had the present disease for two and a half years.

On the left temple, just in front of the ear, there is an irregularly round granulomatous area about 1½ inches (3.8 cm.) in diameter. The area is raised, crusted and fissured. In some areas about the margin there is a flat, erythematous, slightly raised border. Hair is growing throughout the area.

The Wassermann and Kahn reactions were negative. Examination of the hair and scales for tinea gave negative results twice. The eruption started following a cut in a barber shop. There is no history of the ingestion of bromides or iodides.

A histopathologic examination by Dr. Charles F. Sims showed the epidermis for the most part to be atrophic. There was a moderately dilated follicle at one end of the section. A sparse cellular reaction, composed for the most part of small round cells, was present in the upper corium. Basophilic degeneration of collagen in the upper corium was noted. The findings were not sufficient for a definite diagnosis.

Three treatments with 75 r of roentgen rays resulted in no improvement. Four injections of bismuth subsalicylate, 2 grains (0.13 Gm.), brought about no improvement. Use of soothing ointments and antiseptic ointments locally has produced no improvement.

DISCUSSION

DR. JOSEPH C. AMERSBACH: A diagnosis of either bromide eruption or epithelioma has to be considered. I should advise the taking of biopsy specimens from two or three different areas and submitting them to several dermatologic pathologists for their opinions.

DR. LESLIE P. BARKER: This circumscribed granulomatous lesion has a raised, firm border with a verrucous center and islands of epithelium in the center of the lesion. I should favor the diagnosis of basal cell epithelioma. Another biopsy should be performed on a specimen from the border of the lesion, and a guinea pig should also be inoculated with material from the tissue. The other diseases I should consider are tuberculosis, blastomycosis and, possibly, bromoderma. Although there is no history of the ingestion of bromides, I think that a determination of the contents of the blood should be made.

DR. RICHARD J. KELLY: I agree with the previous speaker, Dr. Barker, but I think that in spite of the serologic reactions the test should be repeated, and I should certainly repeat the biopsies. There is a distinct possibility that it is a tertiary syphilitic manifestation. I am more in favor, however, of a mixed baso-squamous epithelioma, because of the time element. I should suggest that if a biopsy is performed an investigation for fungous infection be made.

DR. J. LOWRY MILLER: I should suggest a test of the blood for arsenic, with the idea that this is Bowen's disease developing in a patient exposed to arsenic in the past. One other possibility I can think of is some form of deep fungous infection. I still favor Bowen's disease as the diagnosis.

DR. ROYAL M. MONTGOMERY: When this man was first seen, the lesion was much more crusted and pyogenic than now. In the last ten days he has been using penicillin ointment, and it certainly has cleared the secondary infection. Underlying all that, there is a slightly raised erythematous border and granulomatous

tissue in the center. I think that another biopsy should be performed. I do not believe that it is a fungous infection. Two examinations have been done, and the results were normal. The absence of plasma cell reaction should rule out a late cutaneous syphilis. There is atrophy in the lesion. Dr. Sims, in his description of the slide, did not offer any real help in the diagnosis.

NOTE.—The second biopsy specimen showed changes typical of Bowen's disease with some basal cell epitheliomatous changes.

Boeck's Sarcoid. Presented by DR. J. LOWRY MILLER.

A. B., aged 21, a single Negro woman, was admitted to Vanderbilt Clinic today, complaining of nodular lesions of two years' duration. The nodules first appeared on the face, increased in number and spread to the arms and legs, and in the past four months they have been appearing on the trunk. She has had a chronic cough for one year and has lost 15 pounds (6.8 Kg.) in weight. A roentgenogram and an examination of the sputum at another hospital were said to be noncontributory.

Examination shows many brownish red pinhead-sized to dime-sized nodules with depressed centers scattered on the eyelids, around the nose and mouth and on the arms, legs and, to a less extent, the trunk. The fingers appear normal.

DISCUSSION

DR. LESLIE P. BARKER: This is one of the most extensive cases of sarcoidosis I have seen, and the patient has both cutaneous and subcutaneous lesions. Some of the lesions show atrophy. She also has a few lesions on the extensor surfaces of the arms that are papular, about the size of a pea, some showing pseudonecrosis in the center, and these look like papular necrotic tuberculids. I am wondering if the patient may not have two types of lesions, and it would be interesting to have a biopsy specimen taken from each type.

DR. ROYAL M. MONTGOMERY: I think that it is an unusual case of sarcoid. As far as therapy is concerned, I believe that one will have difficulty in bringing about a cure.

DR. J. LOWRY MILLER: I think that this case, which I saw for the first time this afternoon, presents all the features of sarcoid, including the Roussy-Darier type of sarcoid. It shows atrophy in the center of the lesions. The tuberculin reaction is said to have been positive. She has lost 15 pounds in weight. I have a feeling that this case represents a sarcoid which is now in the stage of passing into active tuberculosis.

Lichen Planus. Presented by DR. J. LOWRY MILLER.

L. G., aged 52, a Negro woman, was admitted to Vanderbilt Clinic on May 21, 1945, with whitish lesions on the buccal mucosa and tongue of three weeks' duration. She had been treated in 1936 for generalized lichen planus.

Examination showed several pea-sized circumscribed macules on the dorsal surface of the tongue. These macules are covered with whitish striations. Similar whitish macules arranged in a fanlike pattern are present on the buccal mucosa.

DISCUSSION

DR. LESLIE P. BARKER: I think that the lesions on the mucous membrane are typical of lichen planus. They are small, milky white, punctate lesions. Some have coalesced to form a lacy mosaic pattern with a shiny surface. The whitish patch lesions on the tongue are also lichen planus. The patient gave a history of having had lichen planus nine years ago, and only two small papules are present now on the arms.

I think that a word of caution about the oral lesions in lichen planus is appropriate. I have seen a prickle cell epithelioma develop in 3 instances on the mucous

membrane at the site of previous lichen planus lesions. One patient was an Irish youth, aged 20, who had had extensive lichen planus on the mouth and body for two years. Prickle cell epithelioma developed on the vermilion border of the lower lip. The other 2 patients were men over 50. One had had lichen planus twenty years previously; the other had had it twenty-five years previously but still had lesions of the mucous membrane, and an epithelioma had developed at the site of the oral lesions.

DR. RICHARD J. KELLY: I agree with Dr. Barker that there were not any cutaneous lesions, but on inquiry the patient gives an obvious history of lichen planus as far back as nine years. I think that the oral lesions are those of lichen planus.

DR. ROYAL M. MONTGOMERY: I also think that this is lichen planus of the mouth. The lesions on the buccal mucosa are typical of this disease. The lesions on the tongue are unusual because they are rarely found. She also has several papules on the wrist typical of lichen planus.

DR. J. LOWRY MILLER: This case was presented because of lesions of the tongue. The rest of the picture is typical. I, too, have seen 1 case in which prickle cell epithelioma developed at the site of recurring lichen planus. I suppose that lichen planus acts as a chronic irritant and leads to the formation of a prickle cell epithelioma.

Pityriasis Rosea. Presented by DR. J. LOWRY MILLER.

F. E., a white woman aged 38, was first seen in Vanderbilt Clinic today. She complained of a generalized, itching eruption of two weeks' duration. She had been given diphenylhydantoin sodium for epileptic seizures beginning six months previously. She has taken the drug for one month.

Examination shows a bright red, macular eruption situated mainly on the trunk but also involving the arms, thighs and neck. Some of the lesions are oval and arranged in the lines of cleavage. The gums are normal.

DISCUSSION

DR. ROYAL M. MONTGOMERY: The eruption is a generalized one. The only disease that it suggests to me is pityriasis rosea, although the lesions were redder than those of this disease. For that reason I believe that diphenylhydantoin sodium, which she has been taking for one month, may be the cause of the present eruption or that it has varied the characteristic picture of pityriasis rosea.

DR. LESLIE P. BARKER: This patient has a great many lesions that resemble pityriasis rosea, especially on the back of the trunk, but she also has dermatitis of the neck and upper part of the chest. Some of the lesions on the arms are bright red and have more the color and appearance of a drug eruption. The patient had taken diphenylhydantoin sodium but shows no reaction in the gums from this drug. She has also taken a cathartic pill, but she did not know whether it contained phenolphthalein.

DR. RICHARD J. KELLY: I favor pityriasis rosea regardless of ingestion of the drug. I think that any one of many drugs can cause an eruption which can resemble pityriasis rosea, but on the left side of the chest of this patient there is a lesion larger than any other lesion, and it resembles the herald patch. Furthermore, the rest of the eruption follows the lines of cleavage. I do not believe that the eruption is anything more than pityriasis rosea.

DR. J. LOWRY MILLER: I presented the case as one of pityriasis rosea and feel that it is probably not due to the ingestion of the drug. There is no evidence of the typical gums often seen after diphenylhydantoin sodium has been taken, although one month may be too short a time for this change to occur. The ingestion of the drug was discontinued as a safeguard.